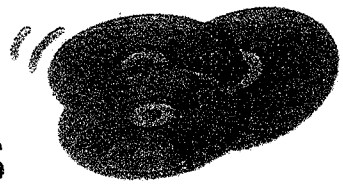
EPA Registration Number

83399-17



NEW APPLICATIONS

DATE: APR 17 2015

FILE REG NUMBER: 83399-RT

FEP (OPPIN ENTRY): LV APR 20 2015

(Initial & Date)

FILE ROOM: _____

(Initial & Date)

SIG: _____

(Initial & Date)

FILE ROOM: _____

(Initial & Date)

ASSIGN TO PM: AD ✓ RD / BPPD _____

_____ **JACKET TO SHELF (DATA)**

REVISED 11/28/12

PROCESSING REQUEST

Reg # 83399-17 **Decision #** 503584

Description: New product registration

Electronic Label & Letter (see PPLS):	OR	**Non Electronic Label & Letter** (Scanning required):
☒ Dated: 2/8/2016		☐ Dated:

Only one label type should be selected

Other Materials Sent (see jacket):

☒ New CSF(s) Dated: 2/4/2016

☐ Other:

File this coversheet and attached materials in the jacket. It must be well organized and clipped together, NOT STAPLED. Then give the jacket with the coversheet and materials to staff in the Information Services Center (ISC) (Room S-4900). If a jacket is full or only available as an image, please file materials in a new jacket and bring it down to the (ISC). For further information please call 703-605-0716.

Reviewer: Rita Kumar

Division: RD

Phone: 703-308-8291 **Date:** 2-25-2016

Kumar, Rita

From:	Kumar, Rita
Sent:	Tuesday, February 23, 2016 10:29 AM
To:	'Katy Hernandez'
Subject:	RE: 83399-17
Attachments:	83399-RT Excerpt of Acute Oral Toxicity and Primary Eye Irritation studies submitted by Ceva 9-24-2015.pdf; 83399-RT product chemistry review.pdf

Katy: See attached chemistry review and excerpt from the acute toxicity review.
Rita

From: Katy Hernandez [mailto:katy.hernandez@ceva.com]
Sent: Monday, February 22, 2016 4:55 PM
To: Kumar, Rita <Kumar.Rita@epa.gov>
Subject: Re: 83399-17

Please accept this email as Ceva's authorization to receive the product chemistry review and acute toxicity reviews by email knowing they contain confidential business information. Thank you for respecting this information as CBI.

Katy Hernandez
Ceva Animal Health, LLC
Regulatory Associate
Development & Regulatory Affairs
8735 Rosehill Rd, Suite 300
Lenexa, KS 66215
913-945-4458

On Mon, Feb 22, 2016 at 3:40 PM, Kumar, Rita <Kumar.Rita@epa.gov> wrote:

This review contains CBI. Please send permission in writing that we can release this information to you by e-mail.

Rita

From: Katy Hernandez [mailto:katy.hernandez@ceva.com]
Sent: Monday, February 22, 2016 4:06 PM

To: Kumar, Rita <Kumar.Rita@epa.gov>
Subject: Re: 83399-17

Is there someone else we could ask for assistance in this situation? Can you extract the reviews of the eye irritation and oral tox? Can you at least forward me the product chemistry review? I'm really sorry to bug you on this, but I am getting a lot of pressure to get state applications submitted. Thank you for any help you can offer.

Katy Hernandez

Ceva Animal Health, LLC

Regulatory Associate

Development & Regulatory Affairs
8735 Rosehill Rd, Suite 300
Lenexa, KS 66215
913-945-4458

On Wed, Feb 17, 2016 at 3:05 PM, Katy Hernandez <katy.hernandez@ceva.com> wrote:

We did submit our own chemistry data and the two acute tox studies. Well, I will take what I can get. As you probably know, California asks for a copy of all EPA reviews of all data submitted.

Katy Hernandez

Ceva Animal Health, LLC

Regulatory Associate

Development & Regulatory Affairs
8735 Rosehill Rd, Suite 300
Lenexa, KS 66215
913-945-4458

On Wed, Feb 17, 2016 at 2:55 PM, Kumar, Rita <Kumar.Rita@epa.gov> wrote:

Not yet. Did you submit your own chemistry data or cite it? Also, I am not sure how I can separate review of the two acute toxicity studies if rest of the data were cited, because there is only one review.

From: Katy Hernandez [mailto:katy.hernandez@ceva.com]
Sent: Wednesday, February 17, 2016 3:48 PM
To: Kumar, Rita <Kumar.Rita@epa.gov>
Subject: Re: 83399-17

Hi Rita, have you had a chance to locate our reviews for the dog product 8339-17?

Katy Hernandez

Ceva Animal Health, LLC

Regulatory Associate

Development & Regulatory Affairs
8735 Rosehill Rd, Suite 300
Lenexa, KS 66215
913-945-4458

On Fri, Feb 12, 2016 at 11:46 AM, Katy Hernandez <katy.hernandez@ceva.com> wrote:

Rita,

I am working to get this product registered in the states, and I need a copy of the reviews for the chemical data and two acute tox studies we submitted. Will you email these reviews at your earliest convenience? Thank you for your help.

Regards,

Katy Hernandez

Ceva Animal Health, LLC

Regulatory Associate

Development & Regulatory Affairs
8735 Rosehill Rd, Suite 300
Lenexa, KS 66215
913-945-4458

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Registration Division (7505P)
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

NOTICE OF PESTICIDE:
_X_ Registration
___ Reregistration

(under FIFRA, as amended)

EPA Reg. Number:	Date of Issuance:
83399-17	2/8/16

Term of Issuance:
Conditional, Time-Limited
Expires: 2/8/2018

Name of Pesticide Product:
Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs

Name and Address of Registrant (include ZIP Code):

Alicia Henk
Director, Development and regulatory Affairs
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with FIFRA section 3(c)(7)(A). You must comply with the following conditions:

1. Submit and/or cite all data required for registration/reregistration/registration review of your product under FIFRA when the Agency requires all registrants of similar products to submit such data.

Signature of Approving Official:	Date:
Venus Eagle, Product Manager 01 Invertebrate-Vertebrate Branch 3, Registration Division (7505P)	2/8/16

EPA Form 8570-6

2. This registration is time-limited and expires 2/8/2018.

3. You must submit quarterly enhanced incident reports and quarterly sales information in doses sold for this product beginning within 3 months of the date the product is first released for shipment, on the first day of the quarter (i.e., January 1, April 1, July 1, or October 1). Please flag any Confidential Business Information as such. Submit enhanced incident reporting and quarterly sales information to the Product Manager's attention. The following is a list of information that must be included in the quarterly reports for each incident:

    - EPA Registration Number
    - Product name (brand name)
    - Lot #
    - Where purchased: internet, store, veterinarian
    - Active Ingredient(s)
    - Weight range for product
    - Date on which incident occurred (mm/dd/yyyy)
    - State in which the incident occurred (standard 2 letter abbreviation)
    - Registrant case #
    - Species: dog, cat, other (specify)
    - Breed: (as reported by pet owner)
    - Age: months or years
    - Sex: M, F, or neutered
    - Weight: pounds
    - Primary Route of Exposure: dermal, oral, other animal, inhalation, other
    - Body System: neurological, dermatological, GI, respiratory, ocular, other
    - Major signs noted with separate column for each sign, using standard terminology
    - Time to Onset: (hours, days)
    - Treated by veterinarian: yes or no
    - First time product used: yes or no
    - Misuse: use on incorrect species, overdose, too frequent dosing, other (describe)
    - Any known precondition
    - EPA Severity Code: death, major, moderate, minor
    - Outcome: died, recovered, still treated, unknown

4. Along with the enhanced incident reporting, you must submit an analysis of the incidents seen, to include the following details:

    - All incidents should be reported including all minor dermal and ocular irritation reports.
    - Summary table for dogs showing number of incidents of each severity code for each route of exposure. Each incident should only be reported once. If one incident has several routes of exposure, the order should be ocular > oral > dermal. In other words, an incident with both oral and dermal exposure would be reported as oral exposure, and an incident with both ocular and oral exposure would be reported as ocular exposure.

- A similar summary table for cats (misuse or secondary exposure) showing number of incidents of each severity code for each route of exposure.
- Summary table for cats and table for dogs showing number of incidents that are believed due to secondary exposure (e.g., multi-pet households).
- A summary table for dogs showing number of incidents for each severity code for these age ranges: <3 months, 3-6 months, 6-9 months, 9-12 months, 1 yr, 2 yr, 3 yr, 4 yr, 5 yr, 6 yr, 7 yr, 8 yr, 9 yr, 10 yr, 11 yr, 12 yr, 13 yr, 14 yr, 15 yr, >15 yr.
- A summary table showing the number of dog incidents for each severity code for each pet weight range on the product label, as applicable.
- A summary table for dog weight showing number of incidents for each product weight range. This table should show number of incidents in dogs weighing less than that product weight range, number of incidents in dogs in lower half of weight range, number of incidents in dogs in upper half of weight range, and dogs weighing more than the product weight range, as applicable.
- Table showing number of incidents for each dog breed, where provided.
- Table showing number of incidents in dogs for each clinical sign.
- Table showing number of incidents in dogs for each organ system.
- Report aggregate incidents, but do not combine moderate and minor incidents.

If EPA determines that future mitigation measures are necessary for all pet spot-ons, the Agency will inform registrants. If mitigation measures are necessary, EPA may take regulatory action.

5. You are required to comply with the data requirements described in the DCI and EDSP Orders identified below:

   a. Imidacloprid GDCI-129099-951
   b. Pyriproxyfen GDCI-129032-1299
   c. Imidacloprid EDSP-129099
   d. Pyriproxyfen EDSP-129032

   You must comply with all of the data requirements within the established deadlines. If you have questions about the Generic DCI or EDSP Order listed above, you may contact the Chemical Review Manager in the Pesticide Reevaluation Division: http://www.epa.gov/oppsrrd1/contacts_prd.htm

6. The data requirements for storage stability and corrosion characteristics (Guidelines 830.6317 and 830.6320) are not satisfied. A one year study is required to satisfy these data requirements. You have 18 months from the date of registration to provide these data.

7. Make the following label changes before you release the product for shipment:

   - Revise the EPA Registration Number to read, "EPA Reg. No. 83399-17."

8. Submit one copy of the final printed label for the record before you release the product for shipment.

Should you wish to add/retain a reference to the company's website on your label, then please be aware that the website becomes labeling under the Federal Insecticide Fungicide and Rodenticide Act and is subject to review by the Agency. If the website is false or misleading, the product would be misbranded and unlawful to sell or distribute under FIFRA section 12(a)(1)(E). 40 CFR 156.10(a)(5) list examples of statements EPA may consider false or misleading. In addition, regardless of whether a website is referenced on your product's label, claims made on the website may not substantially differ from those claims approved through the registration process. Therefore, should the Agency find or if it is brought to our attention that a website contains false or misleading statements or claims substantially differing from the EPA approved registration, the website will be referred to the EPA's Office of Enforcement and Compliance.

If you fail to satisfy these data requirements, EPA will consider appropriate regulatory action including, among other things, cancellation under FIFRA section 6(e). Your release for shipment of the product constitutes acceptance of these conditions. A stamped copy of the label is enclosed for your records.

Please note that the record for this product currently contains the following CSFs:

- Basic CSF dated 2/4/2016

If you have any questions, please contact Rita Kumar by phone at (703) 308-8291, or via email at kumar.rita@epa.gov.

Enclosure: Stamped label

EPA REG. NO. 83399-RT
INITIAL PRODUCT REGISTRATION
DATE: Feb. 08, 2016

> ***"Master Label"***
> *This master label includes label text for different size packages and application rates specific to the pet's age and body weight. Text that appears in parenthesis are informational to the EPA, but will not be printed. Text that appears in brackets are optional.*

FRONT PANEL

(Market Label-

- *The word Dog will be at least 40-75% in height of the largest letter in the primary brand name.*
- *A large clear picture of a dog in the respective weight range will be on the front panel of the label.)*

Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs

Alternate Brand Names include:
Combiva II For Dogs and Puppies
CrossBlock II For Dogs and Puppies
CAH16 for Dogs and Puppies
(The above brand names will be packaged in the weight ranges below:)
3-10 lbs, 7 weeks or older (0.014 fl oz)
11-20 lbs, 7 weeks or older (0.034 fl oz)
21-55 lbs, 7 weeks or older (0.085 fl oz)
Over 55 lbs, 7 weeks or older (0.135 fl oz)

ACCEPTED
Feb 08, 2016
Under the Federal Insecticide, Fungicide and Rodenticide Act as amended, for the pesticide registered under EPA Reg. No. 83399-17

Imidacloprid and Pyriproxyfen Spot-on Solution for Dogs Treats and Prevents Further Flea Infestation on Dogs and puppies 7 weeks and older

ACTIVE INGREDIENTS:	
Imidacloprid	9.10%
Pyriproxyfen	0.46%
OTHER INGREDIENTS:	90.44%
TOTAL	100.00%

NET CONTENTS: **XXX fl oz (XXX mL)**
[XX Doses [each dose XXX fl oz]]

EPA Est. No. TBD **EPA Reg. No. 83399—NEW**

KEEP OUT OF REACH OF CHILDREN

CAUTION

See Back Panel / Package Insert for additional Precautionary Statements, First Aid and Directions for Use.

Use only on dogs [and puppies] weighing (insert product weight range) lbs. and 7 weeks of age or older

"Do Not Use on Cats" icon, (1.5cm x 1.5cm) (placed on front panel)

BACK PANEL & INSERT LANGUAGE

READ ENTIRE LABEL BEFORE EACH USE
USE ONLY ON DOGS AND PUPPIES 7 WEEKS OR OLDER WEIGHING AT LEAST 3 LBS

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS

CAUTION: Harmful if swallowed. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash hands thoroughly with soap and warm water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Keep out of reach of children.

HAZARDS TO DOMESTIC ANIMALS

FOR EXTERNAL USE ON DOGS ONLY. DO NOT USE ON CATS.

Do not use on puppies under 7 weeks of age or weighing less than 3 lbs. As with any product, consult your veterinarian before using this product on medicated, debilitated, aged, pregnant or nursing dogs. If your dog is exhibiting signs or is being treated for skin dermatitis, talk to your vet before applying any topical flea and tick control product.

FIRST AID	
IF SWALLOWED:	Call a poison control center or doctor immediately for treatment advice. Have a person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by the poison control center or doctor. Do not give anything to an unconscious person.
IF IN EYES:	Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.
IF ON SKIN OR CLOTHING:	Wash with plenty of soap and water. Remove and wash contaminated clothing before reuse.
Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may contact 1-800-999-0297 weekdays between 9am and 6pm EST or 1-888-426-4435 for emergency medical treatment information.	

Side Effects: Monitor your dog after application. Side effects, although rare, may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as vomiting or diarrhea have also been reported. If these or other side effects occur, consult your veterinarian or call 1-800-999-0297. Have the product container or label with you when calling your veterinarian for advice.

Keep cats away from treated dog for 24 hours. If applied to a cat or ingested by a cat, contact your veterinarian.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

CONSUMER INFORMATION

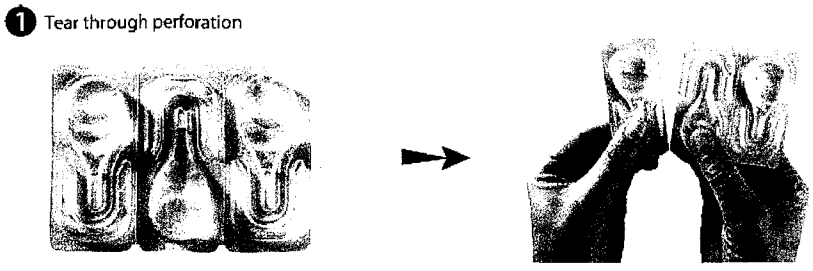
[Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs kills fleas within 12 hours. **Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs** prevents flea infestation for four (4) weeks [1 month] [30 days]. [The active ingredients in Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs [this product] are formulated for control of fleas for 1 month [4 weeks] [30days] on dogs.]

RESTRICTIONS:

- Do not allow children to apply product.
- For use only on dogs [and puppies] 7 weeks and older.
- Do not use on other animals.
- Do not apply to dogs or puppies weighing less than 3 lbs. (0.014 fl. oz.) [11 lbs. (0.034 fl. oz.)] [21 lbs. (0.085 fl. oz.)] [55 lbs. (0.135 fl. oz.)]
- Weigh your dog to be sure you are using the right size product for your dog.
- Do not apply more than one [1] tube per treatment.
- Do not split one tube between two dogs.
- Do not treat your dog with more than one pesticide product at a time. Over dosing your dog can result in serious illness and even death.
- Do not have contact or allow children to have contact with treated area until completely dry.

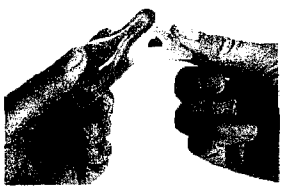
TO PREVENT HARM TO YOU AND YOUR DOG, READ ENTIRE LABEL BEFORE EACH USE. FOLLOW ALL DIRECTIONS AND PRECAUTIONARY STATEMENTS CAREFULLY. FOR EXTERNAL USE ON DOGS ONLY. DO NOT USE ON CATS. DO NOT USE ON OTHER ANIMALS.

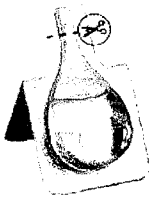
OPENING INSTRUCTIONS:



2 Fold back the safety tab

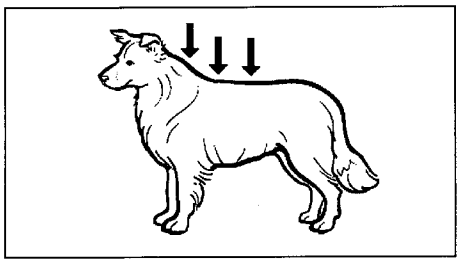
3 Cut with scissors to open applicator





HOW TO APPLY:

1. The dog should be standing or in a comfortable position for easy application. Apply the entire contents of the applicator evenly to three spots along the dog's back, from the shoulder to the middle of the back.
2. At each spot, part the hair down to the level of the skin and gently squeeze the applicator to apply the product. [Avoid superficial application to the dog's hair.]



3. Do not apply an excessive amount of solution to any one spot. This could cause the product to run off the dog. Do not get the product in the dog's eyes or mouth or allow your dog to ingest the product. Do not use more than one tube on dogs greater than 55 lbs.
4. Discard the empty applicator as outlined in the Storage and Disposal section.
5. Repeat every month, or as recommended by your veterinarian.

FREQUENCY OF APPLICATION

Treatment of Imidacloprid and Pyriproxyfen Spot-on Solution for Dogs will kill fleas on dogs [and][puppies] within 12 hours and re-infestating fleas within 2 hours. It is possible pre-existing pupae in the environment may continue to emerge for six [6] weeks [or longer] depending on climatic conditions. Use Imidacloprid and Pyriproxyfen Spot-on Solution for Dogs monthly [every 30 days] [every 4 weeks] for the control and prevention of flea re-infestations.

OR

[Studies have shown that] Imidacloprid and Pyriproxyfen Spot-on Solution for Dogs kills fleas on dogs within 12 hours for up to four [4] weeks [1 month] [30 days]. To prevent flea re-infestation, apply monthly. Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs remains effective even after exposure to sunlight. Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs is water resistant and is still effective, after bathing or water immersion. Allow treated area to dry thoroughly.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

PESTICIDE STORAGE: Store in a cool, dry place. Keep out of reach of children.

PESTICIDE DISPOSAL AND CONTAINER HANDLING: Non-refillable container. Do not reuse or refill this container. **If empty:** Place in trash or offer for recycling, if available. **If partly filled:** Call your local solid waste agency for disposal instructions. Never place unused product down any indoor or outdoor drain.

LIMITED WARRANTY AND LIMITATION OF DAMAGES

Seller warrants that the material conforms to the chemical parameters of the US EPA registration and the label. To the extent consistent with applicable law, seller makes no warranty, express or implied, other than indicated on the label. Buyer and user assume all risk of use and handling of this material. To the extent consistent with applicable law, any damages arising from use of this product or a breach of this warranty shall be limited to direct damages and shall not include consequential or incidental damages such as loss of profit or values.

[Made in Germany]

[Distributed by:] [Manufactured by:]
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

EPA Reg. No. **83399**-NEW
EPA Est. No. **TBD**
[lot#, date &/or label code] [UPC CODE]

Optional Marketing Claims

(for use on the front, side, or back panels of the outer box or on the package insert)

Fleas

- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] contains the active ingredient [imidacloprid,][and an/the] [insect growth regulator][IGR] pyriproxyfen]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] contains an [insect growth regulator] [IGR] that effectively kills flea eggs
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] prevents further flea infestation for four [4] weeks [1 month] [30 days]
- Protects against fleas for up to four [4] weeks [1 month] [30 days]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] helps prevent further flea re-infestation for up to four [4] weeks [1 month] [30 days]
- Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs [continually] works to prevent further flea infestation for up to four [4] weeks [1 month] [30 days]
- Effectively kills adult fleas and prevents further infestation on dogs over 7 weeks of age weighing at least 3 pounds [lbs]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] treats, controls, and prevents further flea infestation
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] treats for fleas within 12 hours on dogs
- Kills fleas within [in] 12 [twelve] hours [after application]
- Kills fleas before egg laying
- Kills fleas before eggs can be laid
- Kills fleas on dogs and puppies 7 weeks of age or older weighing at least 3 pounds [lbs]
- Kills re-infesting fleas within 2 hours
- Kills fleas and their eggs
- Effectively kills flea eggs
- Disrupts the flea cycle and kills larval flea stages
- Breaks the flea life cycle and [prevents] [stops] flea eggs [and larvae] from developing into adult [biting] fleas
- Stops flea eggs from hatching [and] [developing into biting adults]
- Larval flea stages are killed after Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs is applied to dogs 7 weeks or older weighing at least 3 pounds [lbs]
- Kills re-infesting fleas within 2 hours [and protects against further flea re-infestation up to four [4] weeks [one month] [30 days]]
- Prevents further re-infestations by killing adult fleas within 12 hours for up to one month [4 weeks] [30

days]
- Controls fleas for dogs and puppies 7 weeks or older and weighing at least 3 pounds [lbs]
- Treats flea infestations on dogs and puppies 7 weeks or older weighing at least 3 pounds [lbs]
- Provides flea protection up to four [4] weeks [one month] [30 days]]
- Controls against [problematic] flea bites
- Kills fleas that may cause Flea Allergy Dermatitis [FAD]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] offers 3-way flea protection that [kills] [controls] [prevents] adults, larvae, and eggs
- [An effective] flea adulticide, larvicide, and ovicide [that [kills][prevents][,treats] [,and] [controls] fleas]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] offers effective multistage flea control
- Effective [once a month] [flea] [protection] [prevention and treatment]
- Effective flea treatment for your dog 7 weeks or older weighing at least 3 pounds [lbs]
- Monthly topical treatment of Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs kills fleas and treats flea infestation for dogs and puppies 7 weeks or older weighing at least 3 pounds [lbs]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] treats for fleas in 12 hours on dogs and puppies 7 weeks or older weighing at least 3 pounds [lbs]
- Monthly treatment prevents further re-infestation and treats fleas on dogs 7 weeks or older weighing at least 3 pounds [lbs]
- [Kills] [Treats] fleas which may serve as intermediate hosts for tapeworm

All Others
- For Dogs and puppies 7 weeks or older weighing at least 3 pounds [lbs]
- For Use on puppies 7 weeks or older weighing at least 3 pounds [lbs]
- For Use on Dogs Only 7 weeks or older weighing at least 3 pounds [lbs]
- Easy to Use Applicator
- Easy to Apply Applicator
- Applies Easily
- Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs recommends monthly treatments
- One Step Flea Prevention for up to four [4] weeks [one month][30 days]
- For Best Results Apply Monthly [every 30 Days] [every [4] [four] weeks]
- For year round protection apply monthly [every [[four] [4] weeks] [30 days]]
- Use Monthly [Every [30 Days] [4] [Four] Weeks] for best results
- Only one treatment needed every month [30 Days] [[4] [Four] Weeks]
- One treatment remains effective for four [4] weeks [1 month] [30days]
- Convenient
- Water-resistant after application
- Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs is waterproof after application
- Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs is effective after [bathing] [shampooing]
- Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs is effective [even] after exposure to rain or sunlight
- Formulated for control of fleas for 1 month [4 weeks] on dogs
- Contains the [same] active ingredients as in [Bayer] Advantage II for Dogs
- Contains the active ingredients [imidacloprid, pyriproxyfen]found in [Bayer] Advantage II for dogs
- Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs is not manufactured or distributed by Bayer [Animal Health]

EPA REG. NO. 83399-RT
INITIAL PRODUCT REGISTRATION
DATE: Feb. 08, 2016

APPLICATOR LABELING

{Front Label}	{Back Label}
Imidacloprid and Pyriproxyfen Spot-on Solution For Dogs [insert wt range] lbs 7 weeks or older Imidacloprid 9.10% Pyriproxyfen 0.46% XXX fl. oz. {label code}	KEEP OUT OF REACH OF CHILDREN CAUTION Read entire label before use. [Use scissors to open.] EPA REG. No. 83399-NEW Lot # (*designation will identify producing establishment*) {label code}

Kumar, Rita

From: Meadows, Sarah
Sent: Thursday, February 11, 2016 11:24 AM
To: OPP RD QAQC; Eagle, Venus; Kumar, Rita
Subject: QAQC Pass 83399-17
Attachments: 83399-17-20160208.pdf

The above product has passed the quality control check. Please print the e-signed letter/e-stamped label (attached), file the hard copy in the jacket, close the action in OPPIN, and return the jacket to the file room. Include the Data Extraction Request Form for the new CSFs. Please notify me when you have closed the action in OPPIN. Your action can not be uploaded to PPLS until it is closed in OPPIN and the file symbol has been converted to a registration number in the system. Thank you.

Kumar, Rita

Resubmission: S 980711 83399-RT

From: Katy Hernandez <katy.hernandez@ceva.com>
Sent: Friday, February 05, 2016 9:45 AM
To: Kumar, Rita; Alicia Henk
Cc: Eagle, Venus
Subject: Re: FW: Pre-decisional letters for 83399-RT and 83399-RA
Attachments: Revised Feb 4 2016 8570-4 Basic CSF for Imidacloprid + PPF Spot-On Solution for Dogs rev1.pdf; 8570-34 Imid + PPF for Dogs.pdf; 8570-35 Data Matrix Imid + PPF for Dogs_revised PUBLIC.pdf; 8570-35 Data Matrix Imid + PPF for Dogs_revised.pdf

Good morning Rita,
I have attached the updated forms for the dog product first. I will send you a separate email with the cat product forms. I have noted some responses in blue text below to offer some further explanation. We hope these updated forms satisfy your requests.

Katy Hernandez
Ceva Animal Health, LLC
Regulatory Associate
Development & Regulatory Affairs
8735 Rosehill Rd, Suite 300
Lenexa, KS 66215
913-945-4458

On Thu, Feb 4, 2016 at 10:26 AM, Kumar, Rita <Kumar.Rita@epa.gov> wrote:

Katy: Please see the following for the data comp issues:

1. You sent us a revised data matrix with additional citations for generic data to support companion animal use. Please send us an updated data citation form with the same date as the data matrix.

Since we are including updated data matrices with the date of 2/4/2016, we have included updated data citation forms with the date of 2/4/2016.

2. The alternate source for imidacloprid is [redacted] active, whereas the basic source is [redacted] Please explain how you made up the difference in active percentage.

We have included updated CSFs with an additional Attachment B that covers the calculations for the actives and solvents. This is similar to how we have completed the CSFs for other Ceva registered products.

3. The Agency used generic data to make the determination that pyriproxyfen was acceptable for companion animal use. Therefore you must cite or submit generic data for this use. As explained by us to you in a conference call two

weeks ago, doing a cite-all for generic data - companion animal use, and making an offer to pay might be the best way for you to address this data gap.

We have included updated data matrices with additional pyriproxyfen data citations to satisfy this request. Since the cite-all method is cost prohibitive for Ceva, we have cited the two studies that are most applicable to companion animal use.

In addition, There is one more label comment for both products: Add these two notes on the front panel of the draft label above product name:

Market label - the word Cat (or Dog) will be at least 40-75% in height of the largest letter in the primary brand name.

Market label - a large clear picture of a cat (or dog) in the respective weight range will be on front panel of the label.

Please submit revised labels, along with revised data matrix and data compensation forms to me ASAP. You must also provide an explanation for #2 above, or delete the alternate source for imidacloprid, and revised your formulator's exemption form accordingly.

Thanks,

Rita

From: Kumar, Rita
Sent: Wednesday, February 03, 2016 4:48 PM
To: 'Katy Hernandez' <katy.hernandez@ceva.com>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>
Subject: FW: Pre-decisional letters for 83399-RT and 83399-RA
Importance: High

Hi Katy: Further to below, the following additional changes need to be made on the dog label (83399-RT).

1. Delete the claim: "Kills (and)(controls) fleas at all life stages" and any other claims that refer to all life stages.

2. Delete the claim: "[Specially] Formulated to target[s] every stage of flea development [to treat and prevent flea infestation].

3. Some optional marketing claims on page 6 have [7 weeks or older] as optional. The age reference cannot be optional, please remove brackets.

4. Delete "irritating" and "annoying" from the claim: "Controls [against] [problematic] [irritating] [annoying] flea bites".

The following changes must be made in the Cat label (83399-RA). Please refer to highlighted copy of the draft dated 1/29/2016:

1. On the front panel, page 1, Over 9 lbs. is missing a bracket.

2. On page 2, under Consumer Information, last sentence, delete "against". This is not appropriate with rest of the sentence, does not read right!

3. On page 4, under How to Apply, make the following changes in items numbers given below:

    5. Delete the second and third sentences, and replace with the original statement: "Repeat every month, or as recommended by your veterinarian." This is more appropriate, since a veterinarian can determine the severity of infestation and specify the frequency of application.

4. On page 6, Delete the claim: "Prevents [re]infestation by killing adult fleas before [they lay eggs][egg laying][eggs can be laid]".

5. In the Other Claims, last bullet on page 7, change "Compare" to "Contains". Compare is not allowed.

Please submit revised labels for both products. We are still working on the data compensation issue for the source products, and will inform you as soon as a decision has been made.

Regards,

Rita

From: Kumar, Rita
Sent: Wednesday, February 03, 2016 11:35 AM
To: 'Katy Hernandez' <katy.hernandez@ceva.com>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>
Subject: RE: Pre-decisional letters for 83399-RT and 83399-RA
Importance: High

Dear Katy: The following changes need to made in the proposed draft dated 1/29/2016. Refer to the highlighted copy for page numbers.

1. You must submit a picture of the cat icon with the language, on page one and elsewhere. It can be in black and white on the draft label, On page provided you specify the size and colors that will be used on the final printed copy.

2. On page 4, under How to Apply, make the following changes in items numbers given below:

1. Change the last part of last sentence to read: "from the shoulder to the middle of back." Also change the graphic accordingly. The third dot must be applied no further than middle of back to prevent ingestion by the animal.

5. Delete the second and third sentences, and replace with the original statement: "Repeat every month, or as recommended by your veterinarian." This is more appropriate, since a veterinarian can determine the severity of infestation and specify the frequency of application.

3. In the Optional marketing claims, sixth bullet on page 5, change "prevents flea infestation" to "prevents further flea infestation". This change must be made elsewhere also, wherever this kind of statement appears. This product only prevents further flea infestation.

4. In the Optional marketing claims, sixth bullet on page 6, delete "[against]". This is not appropriate with rest of the sentence, does not read right!

5. In the Other Claims, eleventh bullet on page 7, delete "Specially". This indicates heightened efficacy, and is a false claim, since there are many other products with same formulation in the market.

6. In the Other Claims, last bullet on page 7, change "Compare" to "Contains". Compare is not allowed.

I may have some more comments, and I will let you know as soon as I hear from the scientists.

Regards,

Rita

From: Katy Hernandez [mailto:katy.hernandez@ceva.com]
Sent: Friday, January 29, 2016 6:13 PM
To: Kumar, Rita <Kumar.Rita@epa.gov>
Cc: Alicia Henk <alicia.henk@ceva.com>; Eagle, Venus <Eagle.Venus@epa.gov>
Subject: Re: Pre-decisional letters for 83399-RT and 83399-RA

We have attached our response to the predecisional letter for the dog product in this email. This response includes the attached updated documents and forms. Please let me know if these also need to be sent in through the front office.

Katy Hernandez

Ceva Animal Health, LLC

Regulatory Associate

Development & Regulatory Affairs
8735 Rosehill Rd, Suite 300
Lenexa, KS 66215
913-945-4458

On Fri, Jan 22, 2016 at 9:20 AM, Kumar, Rita <Kumar.Rita@epa.gov> wrote:

Dear Alicia and Katy: Please see attached pre-decisional letters for these two spot-on products. Best Regards,

Rita

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
1200 Pennsylvania Avenue, N.W.
WASHINGTON, D.C. 20460

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215	EPA Registration Number/File Symbol 83399-RT
Active Ingredient(s) and/or representative test compound(s) Imidacloprid, Pyriproxyfen	Date 02/04/2016
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) Indoor non-food	Product Name Imidacloprid & Pyriproxyfen Spot-On Solution for Do

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).	☑ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses .

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (I) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
Alicia Henk	02/04/2016	Alicia Henk, Director, Development & Reg. Affairs

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

Date: February 4, 2016	**EPA Reg No./File Symbol:** 83399-NEW	Page 1 of 3
Applicant's/Registrant's Name & Address Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215	**Product:** Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs	
Ingredients: Imidacloprid, Pyriproxyfen		

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Product Chemistry					
830.1550, 830.1600, 830.1620, 830.1650, 830.1670, 830.1750	Group A Product Chemistry for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609001	Ceva Animal Health, LLC	OWN	
830.1800	Assay Determination of Imidacloprid and Pyriproxyfen in Imidacloprid 9.1% (w/w) and Pyriproxyfen 0.46% (w/w) Spot-On Solution	49609002	Ceva Animal Health, LLC	OWN	
830.1800	Assay Determination of Imidacloprid and Pyriproxyfen in Imidacloprid 9.1% (w/w) and Pyriproxyfen 0.46% (w/w) Spot-On Solution: Analytical Method Validation Report	49609003	Ceva Animal Health, LLC	OWN	
830.6302, 830.6303, 830.6304, 830.6313, 830.6314, 830.6315, 830.6316, 830.6319, 830.6321, 830.7000, 830.7100, 830.7300. 830.7520	Summary of Group B Product Chemistry and Waivers for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609004	Ceva Animal Health, LLC	OWN	
830.6302, 830.6303, 830.6304, 830.7100, 830.7300	Physical and Chemical Characteristics: Color, Physical State, Odor, Viscosity, and Density for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609005	Ceva Animal Health, LLC	OWN	
830.6315	Flashpoint for Ceva Animal Health's Imidacloprid Spot-On Solution, Imidacloprid & Pyriproxyfen Spot-On Solution, and Imidacloprid & Permethrin Spot-On Solution	49609006	Ceva Animal Health, LLC	OWN	
Toxicology Data Requirements					
870.1100	Acute Oral Toxicity Study of Imidacloprid Pyriproxyfen Spot On Solution in Sprague-Dawley Rats	49609007	Ceva Animal Health, LLC	OWN	
870.1200	Acute Dermal Toxicity Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096905	Bayer Animal Health	OLD	
870.1300	Acute Four-Hour Inhalation Toxicity Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096906	Bayer Animal Health	OLD	
870.2400	Acute Eye Irritation Test of Imidacloprid/Pyriproxyfen Spot On Solution in New Zealand Albino Rabbits	49609008	Ceva Animal Health, LLC	OWN	
870.2500	Primary Dermal Irritation Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096908	Bayer Animal Health	OLD	

Signature	**Name and Title**	**Date**
Alicia Henk	Alicia Henk, Director Pharmaceutical Development and Regulatory Affairs, Ceva Animal Health, LLC	**February 4, 2016**

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

Date: February 4, 2016	**EPA Reg No./File Symbol:** 83399-NEW	Page 2 of 3
Applicant's/Registrant's Name & Address Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215	**Product:** Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs	

Ingredients: Imidacloprid, Pyriproxyfen

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.2600	Dermal Sensitization Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096909	Bayer Animal Health	OLD	
870.7200	Evaluation of the General Safety of 9.1% Imidacloprid with 0.9% Pyriproxyfen Spot On Formulation in the Target Species, Seven Week Old Puppies	45097101	Bayer Animal Health	OLD	
870.7200	Evaluation of the General Safety of 9.1% Imidacloprid with 0.9% Pyriproxyfen Spot On Formulation in the Target Species, Adult Dogs	45097102	Bayer Animal Health	OLD	
870.7200	Acute Toxicity Evaluation for Dermal Treatment of Dogs with Imidacloprid (Bay t 7391) Spot-on: Lab Project Number: 74580: TR-94D-010. Unpublished study prepared by Miles Inc. 19 p.	43679607	Bayer Animal Health	OLD	
870.7200	General Safety Evaluation for Topical Use of Imidacloprid (Bay t 7391) Spot-On On Dogs: Lab Project Number: 74590: TR-95D-005. Unpublished study prepared by Bayer Corp. 40 p.	43679608	Bayer Animal Health	OLD	
870.7200	General Safety Evaluation for Topical Use of Imidacloprid (Advantage) Spot-On on Puppies: Lab Project Number: TR-96D-003: 74730: 10332. Unpublished study prepared by Bayer Corp. 47 p.	44099801	Bayer Animal Health	OLD	
870.7200	Acute Oral Toxicity Evaluation of Imidacloprid (Advantage) in Dogs: Lab Project Number: TR-96D-010: 74764: J:USERS\LINDA\NOREPORT\JAS0171.RPT. Unpublished study prepared by Bayer Corp., Animal Health. 10 p.	44179801	Bayer Animal Health	OLD	
Product Performance Test Guidelines					
810.3300	Efficacy Evaluation of Bay t 7391 (Imidacloprid) 10% Solution Applied Dermally for Control of Fleas on Dogs	43679609	Bayer Animal Health	OLD	
810.3300	Efficacy Confirmation of NTN 33893 (Imidacloprid) Solution Applied Dermally for Control of Fleas on Dogs	43679610	Bayer Animal Health	OLD	

Signature	**Name and Title** Alicia Henk, Director Pharmaceutical Development and Regulatory Affairs, Ceva Animal Health, LLC	**Date** **February 4, 2016**

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

Date: February 4, 2016		**EPA Reg No./File Symbol**: 83399-NEW	Page 3 of 3
Applicant's/Registrant's Name & Address Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215		**Product:** Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs	
Ingredients: Imidacloprid, Pyriproxyfen			

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Comparative Evaluation of How Quickly Advantage and Frontline (Fipronil) Top Spot Kill Fleas on Dogs: (Final Report)	44256901	Bayer Animal Health	OLD	
810.3300	Imidacloprid Topical Formulation: Larvicidal Effect Against Ctenocephalides felis in the Surroundings of Treated Dogs	44256902	Bayer Animal Health	OLD	
810.3300	Evaluation of the Effects of Shampooing or Water Immersion on the Initial and Residual Efficacy of Advantage for Flea Control on Dogs	44256903	Bayer Animal Health	OLD	
810.3300	Nylar 50 (percent) Concentrate: Product Performance/Efficacy Reports. Unpublished study prepared by McLaughlin Gormley King. 79 p.	45086801	McLaughlin Gormley King Company	OLD	
Imidacloprid and Pyriproxyfen Generic Data for Companion Animal Use					
875.1200, 875.2100, 875.2400	Evaluation of Potential Exposures to Pet Owners and Veterinary Professionals During Application of ADVANTAGE to Control Fleas on Cats and Dogs: Lab Project Number: 106743. Unpublished study prepared by Bayer Corp. 50 p.	43790701 imidacloprid	Bayer Healthcare, LLC	OLD	
	Imidacloprid (Bay t 7391) – Stroke Test in Dogs after Topical Application of Imidacloprid Spot-on 10%; Bayer Animal Health Development AH-D ID: 16051; Unpublished study		Bayer Healthcare, LLC	PAY	
	Evaluation of the Toxicology and Potential Health Risks Associated with Indoor, Nonfood Uses of Sumilarv; J. Driver, S. Oonnithan, O. Paynter, et al. (1991) Unpublished study prepared by Technology Services Group, Inc. 71 p.	42182701 pyriproxifen	McLaughlin Gormley King Company	OLD	
870.3200	S31183: Toxicity Study by Oral (Capsule) Administration to Beagle Dogs for 52 Weeks (Sumilarv Technical Grade): Lab Project Number: 91/0776. Unpublished study prepared by Life Science Research Ltd. 320 p.	42178309 pyriproxifen (on Sumilarv Technical Grade)	McLaughlin Gormley King Company	OLD	

Signature	Name and Title	Date
Alicia Henk	Alicia Henk, Director Pharmaceutical Development and Regulatory Affairs, Ceva Animal Health, LLC	February 4, 2016

Kumar, Rita

From: Eagle, Venus
Sent: Wednesday, February 03, 2016 10:29 AM
To: Kumar, Rita; Backus, Byron
Cc: Redden, John
Subject: RE: Pre-decisional letters for 83399-RT and 83399-RA

Hi Rita and Byron,

I spoke with OGC yesterday about this issue and Mark Dyner said, "either we must have used something to come to the conclusion that using this a.i. was acceptable for companion animal use" or it is a data gap. So if the subchronic and oral capsule feeding was used as part of the generic data for pyriproxyfen to generate the NOEL for mammalian species – then that is the generic data/basis for which we have continued to grant use of this a.i. in pet spot on's regardless of if the percentage of pyriproxyfen is 4.15% or 15% correct? This is the data that needs to be listed on the data matrix selectively or the cite-all for companion animal use.

Many thanks,

Venus Eagle
Product Manager 1
Invertebrate & Vertebrate Branch 3
Registration Division, Office of Pesticide Programs
US EPA (Mail Code 7505P)
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Phone: 703.308.8045

From: Kumar, Rita
Sent: Wednesday, February 03, 2016 9:56 AM
To: Backus, Byron <Backus.Byron@epa.gov>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>; Redden, John <Redden.John@epa.gov>
Subject: RE: Pre-decisional letters for 83399-RT and 83399-RA
Importance: High

Byron: **Thanks a lot for your quick response.** I will take this to mean that a dermal transfer study or citation is not required for pyriproxyfen in these or similar spot-on products, where pyriproxyfen is present at 4.1% in the formulation.

Venus: Let me know if you do not agree with my conclusion.
Rita

From: Backus, Byron
Sent: Wednesday, February 03, 2016 9:39 AM
To: Kumar, Rita <Kumar.Rita@epa.gov>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>; Redden, John <Redden.John@epa.gov>
Subject: RE: Pre-decisional letters for 83399-RT and 83399-RA

As I remember only one pesticide transfer study from pets to humans (or the equivalent) has been done on an active ingredient (not pyriproxyfen). As far as pyriproxyfen is concerned, there was a subchronic (1 year) oral (capsule feeding) study on dogs that was done a number of years ago; the NOEL was 100 mg/kg/day, and I have accepted references to

that study as indicating an acceptably low level of toxicity to mammalian species involved with the use on pets (particularly so as pyriproxyfen-containing pet products have a low percentage – usually less than 2% - of pyriproxyfen). If there are concerns as to what the exact margins of exposure/safety (or whatever terminology is being used now) are associated with use on pets and secondary exposure to children then these values should be calculated by HED. For what it is worth, BPPD registered at least 2 products containing pyriproxyfen for use on pets a number of years ago without even asking for companion animal safety data.

From: Kumar, Rita
Sent: Wednesday, February 03, 2016 8:21 AM
To: Backus, Byron <Backus.Byron@epa.gov>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>
Subject: FW: Pre-decisional letters for 83399-RT and 83399-RA
Importance: High

Hi Byron: Venus and I came to see you yesterday, but you were not in your cubicle at that time. I think Venus has had this discussion with you before also. To the best of your knowledge, do you know of any dermal transfer studies done on pyriproxyfen? We have a dilemma in that none of the pyriproxyfen source products have companion animal use on the technical label, and registrant claims that these sources have been used for formulation into pet spot on products before. Registrant (Ceva) is not giving us any data citations for pyriproxyfen generic data for use on companion animals. So, we must rely on your expertise, wisdom and knowledge!

Registrant claims: "We are not aware that EPA has required any dermal transfer data for companion animal products containing the actives in our end use product." We need to confirm this with you regarding pyriproxyfen. Registrant has revised the CSF and [redacted] is the new source for pyriproxyfen.

Please feel free to refer to the Final Response document among the attachments above, and look at the pyriproxifen source products discussion for more details. I am also copying the text below for your convenience, but it is not easy to read in this copying because the formatting did not copy. The PRIA date is next Monday, so if you can respond this morning, that will be great.

Thanks,
Rita

[redacted]

Product ingredient source information may be entitled to confidential treatment

Pages 31-33 Claimed confidential by submitter

Kumar, Rita

From: Kumar, Rita
Sent: Wednesday, February 03, 2016 9:56 AM
To: Backus, Byron
Cc: Eagle, Venus; Redden, John
Subject: RE: Pre-decisional letters for 83399-RT and 83399-RA

Importance: High

Byron: **Thanks a lot for your quick response.** I will take this to mean that a dermal transfer study or citation is not required for pyriproxyfen in these or similar spot-on products, where pyriproxyfen is present at 4.1% in the formulation.

Venus: Let me know if you do not agree with my conclusion.
Rita

From: Backus, Byron
Sent: Wednesday, February 03, 2016 9:39 AM
To: Kumar, Rita <Kumar.Rita@epa.gov>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>; Redden, John <Redden.John@epa.gov>
Subject: RE: Pre-decisional letters for 83399-RT and 83399-RA

As I remember only one pesticide transfer study from pets to humans (or the equivalent) has been done on an active ingredient (not pyriproxyfen). As far as pyriproxyfen is concerned, there was a subchronic (1 year) oral (capsule feeding) study on dogs that was done a number of years ago; the NOEL was 100 mg/kg/day, and I have accepted references to that study as indicating an acceptably low level of toxicity to mammalian species involved with the use on pets (particularly so as pyriproxyfen-containing pet products have a low percentage – usually less than 2% - of pyriproxyfen). If there are concerns as to what the exact margins of exposure/safety (or whatever terminology is being used now) are associated with use on pets and secondary exposure to children then these values should be calculated by HED. For what it is worth, BPPD registered at least 2 products containing pyriproxyfen for use on pets a number of years ago without even asking for companion animal safety data.

From: Kumar, Rita
Sent: Wednesday, February 03, 2016 8:21 AM
To: Backus, Byron <Backus.Byron@epa.gov>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>
Subject: FW: Pre-decisional letters for 83399-RT and 83399-RA
Importance: High

Hi Byron: Venus and I came to see you yesterday, but you were not in your cubicle at that time. I think Venus has had this discussion with you before also. To the best of your knowledge, do you know of any dermal transfer studies done on pyriproxyfen? We have a dilemma in that none of the pyriproxyfen source products have companion animal use on the technical label, and registrant claims that these sources have been used for formulation into pet spot on products before. Registrant (Ceva) is not giving us any data citations for pyriproxyfen generic data for use on companion animals. So, we must rely on your expertise, wisdom and knowledge!

Registrant claims: "We are not aware that EPA has required any dermal transfer data for companion animal products containing the actives in our end use product." We need to confirm this with you regarding pyriproxyfen. Registrant has revised the CSF and [redacted] is the new source for pyriproxyfen.

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Product ingredient source information may be entitled to confidential treatment

Please feel free to refer to the Final Response document among the attachments above, and look at the pyriproxifen source products discussion for more details. I am also copying the text below for your convenience, but it is not easy to read in this copying because the formatting did not copy. The PRIA date is next Monday, so if you can respond this morning, that will be great.

Thanks,
Rita

[redacted]

* Claimed confidential by submitter*

Pages 36-38 Claimed confidential by submitter

Kumar, Rita

From: Kumar, Rita
Sent: Wednesday, February 03, 2016 9:56 AM
To: Backus, Byron
Cc: Eagle, Venus; Redden, John
Subject: RE: Pre-decisional letters for 83399-RT and 83399-RA

Importance: High

Byron: **Thanks a lot for your quick response.** I will take this to mean that a dermal transfer study or citation is not required for pyriproxyfen in these or similar spot-on products, where pyriproxyfen is present at 4.1% in the formulation.

Venus: Let me know if you do not agree with my conclusion.
Rita

From: Backus, Byron
Sent: Wednesday, February 03, 2016 9:39 AM
To: Kumar, Rita <Kumar.Rita@epa.gov>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>; Redden, John <Redden.John@epa.gov>
Subject: RE: Pre-decisional letters for 83399-RT and 83399-RA

As I remember only one pesticide transfer study from pets to humans (or the equivalent) has been done on an active ingredient (not pyriproxyfen). As far as pyriproxyfen is concerned, there was a subchronic (1 year) oral (capsule feeding) study on dogs that was done a number of years ago; the NOEL was 100 mg/kg/day, and I have accepted references to that study as indicating an acceptably low level of toxicity to mammalian species involved with the use on pets (particularly so as pyriproxyfen-containing pet products have a low percentage – usually less than 2% - of pyriproxyfen). If there are concerns as to what the exact margins of exposure/safety (or whatever terminology is being used now) are associated with use on pets and secondary exposure to children then these values should be calculated by HED. For what it is worth, BPPD registered at least 2 products containing pyriproxyfen for use on pets a number of years ago without even asking for companion animal safety data.

From: Kumar, Rita
Sent: Wednesday, February 03, 2016 8:21 AM
To: Backus, Byron <Backus.Byron@epa.gov>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>
Subject: FW: Pre-decisional letters for 83399-RT and 83399-RA
Importance: High

Hi Byron: Venus and I came to see you yesterday, but you were not in your cubicle at that time. I think Venus has had this discussion with you before also. To the best of your knowledge, do you know of any dermal transfer studies done on pyriproxyfen? We have a dilemma in that none of the pyriproxyfen source products have companion animal use on the technical label, and registrant claims that these sources have been used for formulation into pet spot on products before. Registrant (Ceva) is not giving us any data citations for pyriproxyfen generic data for use on companion animals. So, we must rely on your expertise, wisdom and knowledge!

Registrant claims: "We are not aware that EPA has required any dermal transfer data for companion animal products containing the actives in our end use product." We need to confirm this with you regarding pyriproxyfen. Registrant has revised the CSF and [redacted] is the new source for pyriproxyfen.

Product ingredient source information may be entitled to confidential treatment

Please feel free to refer to the Final Response document among the attachments above, and look at the pyriproxifen source products discussion for more details. I am also copying the text below for your convenience, but it is not easy to read in this copying because the formatting did not copy. The PRIA date is next Monday, so if you can respond this morning, that will be great.

Thanks,
Rita

[redacted]

Pages 41-43 Claimed confidential by submitter

Kumar, Rita

Resubmission: S 980580 77

From: Katy Hernandez <katy.hernandez@ceva.com>
Sent: Friday, January 29, 2016 6:13 PM
To: Kumar, Rita
Cc: Alicia Henk; Eagle, Venus
Subject: Re: Pre-decisional letters for 83399-RT and 83399-RA
Attachments: Cover Letter for Response 29Jan2016- Dog 83399-RT.pdf; Final Response Document Dog.pdf; Revised 1-28-2016 8570-4 Basic CSF for Imidacloprid + PPF Spot-On Solution for Dogs.pdf; 20160125 8570-35 Data Matrix Imid + PPF for Dogs_revised.pdf; 20160125 8570-35 Data Matrix Imid + PPF for Dogs_PUBLIC_revised.pdf; Revised 1-28-2016 8570-27 Imid + PPF for Dogs.pdf; Imidaclprid + PPF Dog Label - Highlighted.pdf; Imidaclprid + PPF Dog Label.pdf

We have attached our response to the predecisional letter for the dog product in this email. This response includes the attached updated documents and forms. Please let me know if these also need to be sent in through the front office.

Katy Hernandez
Ceva Animal Health, LLC
Regulatory Associate
Development & Regulatory Affairs
8735 Rosehill Rd, Suite 300
Lenexa, KS 66215
913-945-4458

On Fri, Jan 22, 2016 at 9:20 AM, Kumar, Rita <Kumar.Rita@epa.gov> wrote:

Dear Alicia and Katy: Please see attached pre-decisional letters for these two spot-on products. Best Regards,

Rita

Pages 45-60 Claimed confidential by submitter

EPA REG. NO. 83399-RT
INITIAL PRODUCT REGISTRATION
DATE: Jan. 29, 2016

Not approved

"Master Label"
(This master label includes label text for different size packages and application rates specific to the pet's age and body weight. Text that appears in parenthesis or brackets is optional.)

FRONT PANEL

Picture of dog/puppy according to weight range

Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs

Alternate Brand Names include:
Combiva II for Dogs and Puppies
CAH16 for Dogs and Puppies
[The above brand names will be packaged in the weight ranges below:]

3-10 lbs, 7 weeks or older (0.014 fl oz)
11-20 lbs, 7 weeks or older (0.034 fl oz)
21-55 lbs, 7 weeks or older (0.085 fl oz)
Over 55 lbs, 7 weeks or older (0.135 fl oz)

Imidacloprid and Pyriproxyfen Spot-on Solution for Dogs Treats and Prevents Further Flea Infestation on Dogs [and puppies 7 weeks and older]

ACTIVE INGREDIENTS:	
Imidacloprid	9.10%
Pyriproxyfen	0.46%
OTHER INGREDIENTS:	90.44%
TOTAL	100.00%

NET CONTENTS: **XXX fl oz (XXX mL)**
[XX Doses [each dose XXX fl oz]]

EPA Est. No. TBD **EPA Reg. No. 83399—NEW**

KEEP OUT OF REACH OF CHILDREN
CAUTION

See Back Panel / Package Insert for additional Precautionary Statements, First Aid and Directions for Use.

Use only on dogs [and puppies] weighing (insert product weight range) lbs. and 7 weeks of age or older

"Do Not Use on Cats" icon, (1.5cm x 1.5cm) [placed on front panel]

EPA REG. NO. 83399-RT
INITIAL PRODUCT REGISTRATION
DATE: Jan. 29, 2016

BACK PANEL & INSERT LANGUAGE

READ ENTIRE LABEL BEFORE EACH USE
USE ONLY ON DOGS

IMPORTANT CONSUMER INFORMATION

[**Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs** kills fleas within 12 hours. **Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs** prevents flea infestation for four (4) weeks [1 month] [30 days]. [The active ingredients in Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs [this product] are formulated for control of fleas for 1 month [4 weeks] [30days] on dogs.]

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS
CAUTION: Harmful if swallowed. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash hands thoroughly with soap and warm water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Keep out of reach of children.

HAZARDS TO DOMESTIC ANIMALS
FOR EXTERNAL USE ON DOGS ONLY. DO NOT USE ON CATS.
Do not use on puppies under 7 weeks of age or weighing less than 3 lbs. As with any product, consult your veterinarian before using this product on medicated, debilitated, aged, pregnant or nursing dogs. If your dog is exhibiting signs or is being treated for skin dermatitis, talk to your vet before applying any topical flea and tick control product.

FIRST AID	
IF SWALLOWED:	Call a poison control center or doctor immediately for treatment advice. Have a person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by the poison control center or doctor. Do not give anything to an unconscious person.
IF IN EYES:	Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.
IF ON SKIN OR CLOTHING:	Wash with plenty of soap and water. Remove and wash contaminated clothing before reuse.
Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may contact 1-800-999-0297 weekdays between 9am and 6pm EST or 1-888-426-4435 for emergency medical treatment information.	

Side Effects: Monitor your dog after application. Side effects, although rare, may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as vomiting or diarrhea have also been reported. If these or other side effects occur, consult your veterinarian or call 1-800-999-0297. Have the product container or label with you when calling your veterinarian for advice.

EPA REG. NO. 83399-RT
INITIAL PRODUCT REGISTRATION
DATE: Jan. 29, 2016

DO NOT USE ON CATS. Keep cats away from treated dog for 24 hours. If applied to a cat or ingested by a cat, contact your veterinarian.

"Do Not Use on Cats" icon, [1.5cm x 1.5cm]

DIRECTIONS FOR USE

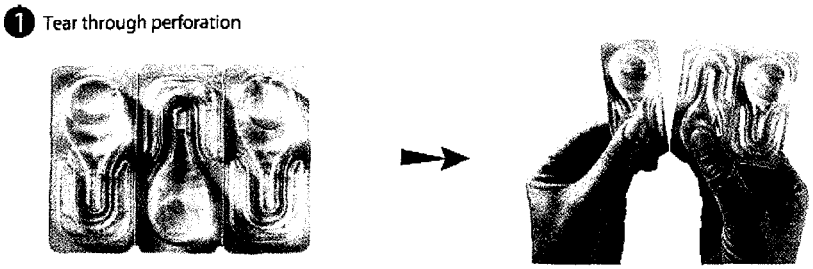
It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

RESTRICTIONS

- Do not allow children to apply product.
- For use only on dogs [and puppies] 7 weeks and older.
- Do not use on other animals.
- Do not apply to dogs or puppies weighing less than 3 lbs. (0.014 fl. oz.) [11 lbs. (0.034 fl. oz.)] [21 lbs. (0.085 fl. oz.)] [55 lbs. (0.135 fl. oz.)]
- Weigh your dog to be sure you are using the right size product for your dog.
- Do not apply more than one [1] tube per treatment.
- Do not split one tube between two dogs.
- Do not treat your dog with more than one pesticide product at a time. Over dosing your dog can result in serious illness and even death.
- Do not have contact or allow children to have contact with treated area until completely dry.

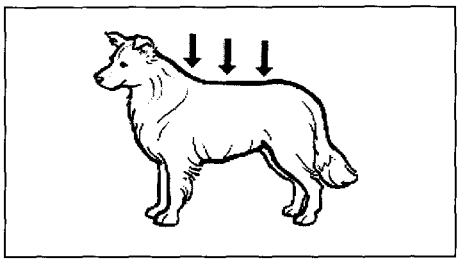
TO PREVENT HARM TO YOU AND YOUR DOG, READ ENTIRE LABEL BEFORE EACH USE. FOLLOW ALL DIRECTIONS AND PRECAUTIONARY STATEMENTS CAREFULLY. FOR EXTERNAL USE ON DOGS ONLY. DO NOT USE ON CATS. DO NOT USE ON OTHER ANIMALS.

OPENING INSTRUCTIONS:



HOW TO APPLY:

1. The dog should be standing or in a comfortable position for easy application. Apply the entire contents of the applicator evenly to three spots along the dog's back, from the shoulder to the base of the tail.
2. At each spot, part the hair down to the level of the skin and gently squeeze the applicator to apply the product. (Avoid superficial application to the dog's hair).



(alternate brand name graphic may vary)

3. Do not apply an excessive amount of solution to any one spot. This could cause the product to run off the dog. Do not get the product in the dog's eyes or mouth or allow your dog to ingest the product. Do not use more than one tube on dogs greater than 55 lbs.
4. Discard the empty applicator as outlined in the Storage and Disposal section.
5. Under normal conditions the product is effective for a month. However, in case of severe flea infestation, retreatment may be necessary earlier than four weeks. Do not re-treat more often than once every seven (7) days. After flea control is obtained, return to a monthly retreatment schedule.

FREQUENCY OF APPLICATION

Treatment of Imidacloprid and Pyriproxyfen Spot-on Solution for Dogs will kill fleas on dogs [and][puppies] within 12 hours and re-infestating fleas within 2 hours. It is possible pre-existing pupae in the environment may continue to emerge for six [6] weeks [or longer] depending on climatic conditions. Use Imidacloprid and Pyriproxyfen Spot-on Solution for Dogs monthly [every 30 days] [every 4 weeks] for the control and prevention of flea re-infestations.

OR

[Studies have shown that] Imidacloprid and Pyriproxyfen Spot-on Solution for Dogs kills fleas on dogs within 12 hours for up to four [4] weeks [1 month] [30 days]. To prevent flea [re]infestation, apply monthly. Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs remains effective even after exposure to sunlight. Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs is water resistant and is still effective, after bathing or water immersion. Allow treated area to dry thoroughly.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

PESTICIDE STORAGE: Store in a cool, dry place. Keep out of reach of children.

PESTICIDE DISPOSAL AND CONTAINER HANDLING: Non-refillable container. Do not reuse or refill this container. **If empty:** Place in trash or offer for recycling, if available. **If partly filled:** Call your local solid waste agency for disposal instructions. Never place unused product down any indoor or outdoor drain.

LIMITED WARRANTY AND LIMITATION OF DAMAGES

Seller warrants that the material conforms to the chemical parameters of the US EPA registration and the label. To the extent consistent with applicable law, seller makes no warranty, express or implied, other than indicated on the label. Buyer and user assume all risk of use and handling of this material. To the extent consistent with applicable law, any damages arising from use of this product or a breach of this warranty shall be limited to direct damages and shall not include consequential or incidental damages such as loss of profit or values.

[Made in Germany]

[Distributed by:] [Manufactured by:]
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

EPA Reg. No. **83399**-NEW
EPA Est. No. **TBD**
[lot#, date &/or label code] [UPC CODE]

Optional Marketing Claims

(for use on the front, side, or back panels of the outer box or on the package insert)

Fleas

- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] contains the active ingredient [imidacloprid],[and an/the] [insect growth regulator][IGR] pyriproxyfen]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] contains an [insect growth regulator] [IGR] that effectively kills flea eggs
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] prevents flea infestation for four [4] weeks [1 month] [30 days]
- Protects against fleas for up to four [4] weeks [1 month] [30 days]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] helps prevent further flea reinfestation for up to four [4] weeks [1 month] [30 days]
- Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs [continually] works to prevent flea infestation for up to four [4] weeks [1 month] [30 days]
- Effectively kills adult fleas and prevents further infestation on the dog
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] treats, controls, and prevents flea infestation
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] treats for fleas within 12 hours on dogs
- Kills fleas within [in] 12 [twelve] hours [after application]
- Kills fleas before egg laying
- Kills fleas before eggs can be laid
- Kills fleas on dogs and puppies

- Kills re-infesting fleas within 2 hours
- Kills fleas and their eggs
- Effectively kills flea eggs
- Disrupts the flea cycle and kills larval flea stages
- Breaks the flea life cycle and [prevents] [stops] flea eggs [and larvae] from developing into adult [biting] fleas
- Stops flea eggs from hatching [and] [developing into biting adults]
- Kills [and] [controls] fleas at all life stages
- Larval flea stages are killed after Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs is applied [to dog]
- Kills flea larval stage after contact [treatment] with Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs
- Prevents [re]infestation by killing adult fleas before [they] [lay eggs] [egg laying] [eggs can be laid]
- Kills re-infesting fleas within 2 hours [and protects against further flea reinfestation up to four [4] weeks [one month] [30 days]]
- Prevents [recurring] [re]infestation[s] by killing adult fleas [within 12 hours] and continues to prevent [re]infestations for up to one month [4 weeks] [30 days]
- Controls fleas for dogs and puppies [7 weeks or older]
- Treats flea infestation [on dogs [and puppies] 7 weeks or older]]
- Provides flea protection up to four [4] weeks [one month] [30 days]]
- Controls against [problematic] [irritating] [annoying] flea bites
- Kills fleas that may cause Flea Allergy Dermatitis (FAD)
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] offers 3-way flea protection that [kills] [controls] [prevents] adults, larvae, and eggs
- [An effective] flea adulticide, larvicide, and ovicide [that [kills][prevents][,treats] [,and] [controls] against fleas]]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] offers effective multistage flea control
- Effective [once a month] [flea] [protection] [prevention and treatment]
- Effective flea treatment [for your dog]
- Monthly topical treatment of Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs kills fleas and treats flea infestation [for dogs [and puppies 7 weeks or older]]
- [[Specially] Formulated to] target[s] every stage of flea development [to treat and prevent flea infestation]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs] treats for fleas in 12 hours on dogs and puppies [7 weeks or older]]
- Monthly treatment prevents further reinfestation and treats fleas on dogs 7 weeks or older
- [Kills] [Treats] [against] fleas which may serve as intermediate hosts for tapeworm

All Others

- For Dogs and puppies 7 weeks or older
- For Use on puppies 7 weeks or older
- For Use on Dogs Only
- Easy to Use [Applicator]
- Easy to Apply [Applicator]
- Applies Easily
- Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs recommends monthly treatments
- Easy One Step Flea Prevention for up to four [4] weeks [one month][30 days]

- For Best Results Apply Monthly [every 30 Days] [every [4] [four] weeks]
- Best used year round [once [a month] every [[four] [4] weeks] [30 days]]
- Use Monthly [Every [30 Days] [4] [Four] Weeks] for best results
- Only one treatment needed every month [30 Days] [[4] [Four] Weeks]
- One treatment remains effective for four [4] weeks [1 month] [30days]
- Convenient
- Water-resistant after application
- Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs is waterproof after application
- Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs is effective after [bathing] [shampooing]
- Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs is effective [even] after exposure to rain or sunlight
- Specially formulated for control of fleas for 1 month [4 weeks] on dogs
- Contains the [exact] [same] active ingredients in [Bayer] Advantage II for Dogs
- Compare the active ingredients [imidacloprid, pyriproxyfen] in [Bayer] Advantage II for dogs
- Imidacloprid and Pyriproxyfen Spot-On Solution for Dogs is not manufactured or distributed by Bayer [Animal Health]

APPLICATOR LABELING

{Front Label}	{Back Label}
Imidacloprid and Pyriproxyfen Spot-on Solution For Dogs [insert wt range] lbs 7 weeks or older Imidacloprid 9.10% Pyriproxyfen 0.46% XXX fl. oz. {label code}	KEEP OUT OF REACH OF CHILDREN CAUTION Read entire label before use. (Use scissors to open.) EPA REG. No. 83399-NEW Lot # (*designation will identify producing establishment*) {label code}

Kumar, Rita

From: Kumar, Rita
Sent: Friday, January 22, 2016 10:20 AM
To: Alicia Henk; Katy Hernandez
Cc: Eagle, Venus
Subject: Pre-decisional letters for 83399-RT and 83399-RA
Attachments: 83399-RT pre-decisional letter signed 1-22-2016.pdf; 83399-RT label comments rk 1-22-2016.docx; 83399-RA predecisional letter signed 1-22-2016.pdf; 83399-RA label comments rk 1-22-2016.docx

Dear Alicia and Katy: Please see attached pre-decisional letters for these two spot-on products. Best Regards, Rita

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
Washington, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

JAN 2 2 2016

Alicia Henk
Sergeant's Pet Care Products, Inc.
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

Subject: PRIA Predecisional letter – New product registration
Product Name: Imidacloprid & Pyriproxifen Spot-On Solution for Dogs
EPA File Symbol: 83399-RT
Decision Number: 503584

Dear Ms. Henk:

The Agency has completed its review and assessment of your application pursuant to Section 33(b)(3) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) as amended by the Pesticide Registration Improvement Extension Act of 2012. The Agency has made a pre-decisional determination that your application cannot be approved unless revisions are made to the draft label dated May 14, 2015. The necessary label changes are specified on the attached document.

Since there is limited time before the PRIA Decision Due Date expires, it is important to discuss any objections you have to these changes immediately and whether you will need to submit additional data for review. If these discussions determine that submitting data will be necessary, the PRIA decision due date may need to be renegotiated to allow sufficient time to address and resolve such differences. If the PRIA Decision Due Date is not renegotiated, and the label issues are not resolved before the PRIA Decision Due Date, the Agency will send a follow-up letter that will represent the Agency's decision to close out the PRIA decision review time. The follow-up letter will provide the following three options for continuing the review of the application:

a. You agree to all of the terms associated with the draft accepted label as revised by the Agency and requests that it be issued as the accepted final Agency-stamped label; or
b. You do not agree to one or more of the terms of the draft accepted label as revised by the Agency and requests additional time to resolve the difference(s); or
c. You withdraw the application without prejudice for subsequent resubmission, but forfeits the associated registration service fee.

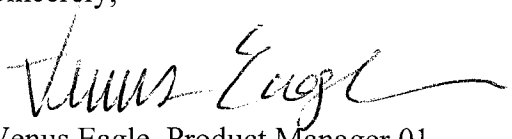
If you inform EPA that you have concerns as described under (b) above, you will have up to 30 calendar days from the date of that follow-up letter to reach agreement with the Agency on the final version of the

label that the Agency will accept. If an agreement cannot be reached within those 30 days, EPA would intend to proceed with denial of the application.

If you agree to all of the terms of the accepted label as described in (a) above, or if you and EPA resolve any differences as described in (b), you must submit a revised label to EPA. EPA will then provide an accepted final Agency stamped label to you within 2 business days following your written electronic confirmation of agreement to the Agency including the revised label to be stamped.

If you have any questions, please contact Rita Kumar at kumar.rita@epa.gov or (703) 308-8291.

Sincerely,



Venus Eagle, Product Manager 01
Invertebrate and Vertebrate Branch 3
Registration Division (7505P)
Office of Pesticide Programs

Attachment (1)

Attachment for Predecisional letter for 83399-RT

Label Comments for 83399-RT (Imidacloprid & Pyriproxifen Spot-On Solution for Dogs)

1. As indicated to you by e-mail on 1/15/2016, the basic Confidential Statement of Formula (CSF) dated 9/1/2016 is not acceptable, because the source products for imidacloprid and pyriproxyfen are not registered for use on companion animals. You must submit a revised data matrix and data citation form after adding cite-all for generic data for companion animal safety, along with a cite-all offer to pay on the data citation form. Alternatively, you can use a source product for each active that is registered for use on companion animals, provided no other changes are made in composition of the basic CSF. A revised Formulator's Exemption statement is needed if you choose this second option.

2. On page 1, change the referral statement as follows: "see Back Panel/Package Insert for additional precautionary statements, First Aid and Directions for Use".

3. The product name must indicate only the basic name that appears on the application form, and will be use in the Notice of Registration, and it is: Imidacloprid and Pyriproxifen Spot-On Solution for Dogs. The alternate brand name can be listed separately under the heading Alternate Brand Name.

4. On page 1, the weight and package size statements must be revised to indicate what package size will be used on what weight animal, remove brackets from these statements. Since you have several package sizes under one registration, the animal's weight must relate to intended package size and minimum age of the animal must be mentioned, none of this can be optional.

5. On page 1, change both intended use statements to read as follows: Imidacloprid and Pyriproxifen Spot-On Solution for Dogs Treats and Prevents Further Flea Infestation on Dogs and....., and remove brackets from the first one. This must not be optional.

6. Across the board, replace [Name of Product] with basic product name.

7. According to the pet spot on mitigation initiative of 2011, draft labels for dogs must indicate cat icons with strike-thru in yellow and black color, and appear in lower right hand corner on the front panel, and with the cat statement elsewhere in the Directions for Use.

8. On page 2, under First Aid, reverse the order of If Swallowed and If In Eyes, to be consistent with toxicity categories assigned to the product.

9. Wherever you are referring to multiple product name, the first option, preferably the primary name must not be brackets indicating optional. Similarly, no part of the statement "within 12 hours" can be optional, this statement must appear in its entirety

to define the time it takes for product to be effective. Similarly, where multiple choices for control time (four weeks, one month etc.) are given, the first one must not be within brackets.

10. We would like to see the graphic for application to animal. Application should only be made upto the middle of back of animal. Dogs are known to lick their tails, thus increasing the chance of ingestion if application is made to base of tail.

11. Delete the following claims related to efficacy of the product. These claims are not supported by cited efficacy data:
    - kills infesting fleas within 2 hours, the 2 hrs apply to reinfestation only. (You have made "re" as optional in a few places, that is not acceptable, and the optional brackets be changed)
    - prevents flea infestation for at least 4 weeks [1 month][30 days], (delete "at least")
    - long lasting control
    - effectively stops [ends] existing flea infestation, ("ends" is not acceptable)
    - kills reinfesting fleas before they can lay eggs
    - effectively controls existing fleas infestation for by killing adult fleas and prevents further infestation in the home, (you can revise this to read as: "effectively kills adult fleas and prevents further reinfestation on the dog")
    - treatment with product can reduce incidence of flea allergic dermatitis (FAD) or flea bite hypersensitivity (this must be superseded with kills fleas that may cause...(FAD)
    - regular monthly use kills fleas and aids in preventing [FAD][flea bite hypersensitivity][from developing]
    - Kills fleas in less than 24 hours, (because it could be interpreted as a time frame less than 12 hours)
    - Treats, controls and prevents flea infestation (change infestation to reinfestation)
    - Treats [controls] and helps prevent further infestation (change infestation to reinfestation)
    - [Effectively] disrupts the flea life cycle and kills flea larval stages (delete effectively)
    - complete [comprehensive] and effective multistage flea protection (complete and comprehensive are heightened efficacy claims, and must be deleted)
    - monthly treatment prevents and treats fleas on dog 7 weeks or older (change this to prevents further reinfestation and treats....)
    - Studies have shown that product kills fleas on dogs within 12 hours for up to 1 month [4 weeks][30 days] before adults start laying eggs (eggs could have been laid prior to application)

12. The following optional marketing claims are acceptable:
    - kills within 12 hours
    - kills reinfesting fleas within 2 hours (note: infesting is not acceptable with the 2 hour timeframe, must always state reinfesting)

- prevents flea infestation for 4 weeks [1 month][30 days] (the first time description cannot be optional, make this change across the board)
- [brand name] is an effective flea adulticide, larvicide, and ovicide that kills [prevents][treats][and][controls] against fleas
- Product is effective after exposure to sunlight, is water resistant, waterproof, and is still effective after bathing, or water immersion.
- To prevent [re]infestation, apply monthly
- Contains the active ingredient imidacloprid and the insect growth regulator, pyriproxyfen
- Contains the IGR that effectively kills eggs
- Protects against fleas [for up to 4 weeks][1 month][30 days]
- Kills fleas in less than 24 hours
- Kills fleas before egg laying
- Kills fleas on dogs and puppies
- Kills fleas and their eggs
- Effectively kills eggs
- Disrupts [breaks] the flea life cycle
- Prevents fleas from developing into biting adults
- Kills [controls] flea life [cycles] [stages]
- Prevents eggs from hatching and developing into biting adults
- Kills larval stages of fleas
- Helps prevent recurring [re] infestations by killing adult fleas [within 12 hours], and continues to prevent [re]infestation for 1 month [4 weeks][30 days] (the 1 month time frame is mandatory here)
- Controls fleas for dogs and puppies
- [Treats] [controls] [prevents] flea infestation
- Provides flea protection [for 1 month][4 weeks][30 days]
- Controls against problematic fleas
- offers 3 way flea protection [kills][controls][prevents] adults, larvae, and eggs
- offers effective multistage control
- formulated to target stages of flea development to treat and prevent flea development
- [kills] [treats][against] fleas which may serve as an intermediate host for tapeworm

The only reference to FAD should be written in the following manner: this product kills fleas that may cause FAD.

13. For the largest size package, there is no upper weight limit, so add this statement to directions for application: "Do not use more than one tube on dogs greater than 55 lbs".

14. Add the following to Restrictions:
    - Do not allow children to apply this product
    - Do not allow your dog to ingest this product

- Do not reapply for four weeks
- Revise the statement "Do not apply to dogs or puppies weighing less than 3 lbs." by adding weight ranges for different size tubes
- Use entire contents of the tube on each dog. Do not split one tube between two dogs. Do not use multiple tubes on one dog
- Weigh your dog to be sure you are using the right size tube for your dog
- Separate your dog from all other dogs and cats for 24 hours after treatment

15. All Restrictions must be indicated as bulleted statements for more prominence

16. Delete the following "Fleas" marketing claims:
    - Complete and effective flea protection
    - Comprehensive and effective flea treatment
    - Contain the same active ingredients in Bayer...., or Compare to Bayer..... Comparative claims are not acceptable.

9. Per the implementation of label changes to pet spot on products in 2011:

a. The Front Panel is to have a large clear picture of a dog in the weight range for the product as packaged;

b. The Back Panel: Place the box labeled "Side Effects" at the lower right hand corner of the back panel.

Kumar, Rita

From: Kumar, Rita
Sent: Friday, January 15, 2016 4:23 PM
To: 'Alicia'; Katy Hernandez
Cc: Eagle, Venus
Subject: RE: New dog and cat spot on applications 83399-RT and 83399-RA

Importance: High

Hi Alicia: Hope you are doing well. There is an issue with these two registrations that need your immediate attention. None of the two source products (for imidacloprid and pyriproxifen) are registered for indoor no-food use on companion aniumals. Therefore, please submit a revised data matrix with cite all generic data citation for companion animals with an offer to pay form. This is to cover any generic data that were submitted for use of these two chemicals on companion animals. Please send us the revised data matrix and data citation form ASAP. We will be sending you label comments next week.
Beast Regards,
Rita

From: Alicia [mailto:alicia.henk@ceva.com]
Sent: Monday, May 11, 2015 4:19 PM
To: Kumar, Rita <Kumar.Rita@epa.gov>; Katy Hernandez <katy.hernandez@ceva.com>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>
Subject: Re: New dog and cat spot on applications 83399-RT and 83399-RA

Hi Rita
I am happy to see winter behind us! Bring on the sunshine!
Thanks for your info. I will review the agency comments tonight and revert asap.

Best regards
Alicia

On May 11, 2015, at 2:57 PM, Kumar, Rita <Kumar.Rita@epa.gov> wrote:

> Dear Alicia: I have not communicated with you in a while. Hope you are doing well and enjoying the spring weather.
>
> I am doing a preliminary screen of these two spot-on applications, and have the following comments on the proposed labels:
>
> 1. Delete "[insert product name]", and add proposed product name on the front panel. This label must refer to the primary brand name.
>
> 2. Most of the brackets on the front panel statements and in optional marketing text are unnecessary or redundant, and make the label very confusing. Please simplify this label.
>
> 3. First Aid and Precautionary Statements are mandatory for both label and package insert. Delete the bracketed text from the two bulleted statements.

4. Delete the Optional text statement right below the two bulleted statements.

5. Delete the 3 optional text statements starting with: :Apply to cats.....". Only the sentence above with both minimum age and min weight are correct.

6. Delete brackets from the heading "[optional Marketing Text]".

7. The marketing text should be moved to end of the label. It should appear after the Precautionary statements and directions for use.

8. Delete "Fast Acting", or define it based on supporting efficacy data.

9. Under Directions for Use, the description of container (tube, via, applicator etc.) must match the picture. We suggest you use the term applicator, and delete other terms.

10. The statement regarding volume and pet weight needs to be clarified to reflect different volume and weight combination.

11. On the application form in column 6, indicate the product which was the basis of your proposed labeling and marketing text.

Please submit revised labels for further consideration of these applications. Since these are e-submissions, the revised labels must be uploaded to Documentum, therefore also be submitted on a CD thru front end with a hard copy of the cover letter explaining the changes, Please respond ASAP, so that the correct label can be sent for review. Thanks.

Regards,
Rita

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: Rita Kumar

From: Jacquelyn Marchese, Entomologist Jacquelyn Marchese

Secondary Review: Kevin Sweeney, Senior Entomologist Kevin J. Sweeney

Date: January 11, 2016

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD (DER)

~~**THIS DER CONTAINS CONFIDENTIAL BUSINESS INFORMATION, AND SHOULD NOT BE RELEASED TO THE REGISTRANT**~~

Note: MRIDs found to be **unacceptable** to support label claims should be removed from the data matrix.

DP barcode: 428211
Decision no.: 503584
Submission no: 968645
Action code: R315
Product Name: Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs
EPA Reg. No or File Symbol: 83399-RT
Formulation Type: liquid pet spot-on
Ingredients statement from the label with PC codes included:
Imidacloprid 9.10% PC: 129032
Pyriproxyfen 0.46% PC: 129099

Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m^2 or mg/cm^2 or mg/kg body weight as appropriate):

Weight range	Monthly product application rate	Lowest imidacloprid mg/kg*	Lowest pyriproxyfen mg/kg*
3-10 lbs (1.36-4.54 kg)	0.4 mL	8.82	0.45
11-20 lbs (4.99-9.07 kg)	1.0 mL	11.0	0.56
21-55 lbs (9.52-24.9 kg)	2.5 mL	10.1	0.51
55+ lbs (24.9+ kg)	4.0 mL	16.0	0.81

*density is 1.1 g/mL

Use Patterns: For monthly use on dogs to provide protection against fleas. Product should be applied evenly to three spots along the dog's back, from the shoulders to the base of the tail. At each spot, part the hair down to the level of the skin and gently squeeze the applicator to apply the product.

I. Action Requested: Review all 6 cited studies and determine their acceptability in support of the proposed product.

II. Background: This proposed product has been given the R315 PRIA designation and is citing 6 efficacy studies to support this product. The 6 cited studies were recently cited to support 2517-RTA. 2517-RTA contains the same percentage of active ingredients that are proposed for this product, 83399-RT. In the 2517-RTA efficacy review dated 11/12/2015 (DP 427198), MRIDs 43679609, 44256902, 44256903, were rated unacceptable, MRID 442569011, 45086801, were rated partially acceptable, and MRID 43679609 was rated acceptable based on today's scientific standards. However, all of these studies are currently supporting claims against public health pests for products 11556-116, and 11556-118, and therefore, similar claims will be supported until all dog products are called in to be reevaluated for registration review.

III. MRID Summary:

As stated above, MRIDs 43679609, 44256902, 44256903, were rated unacceptable, MRID 442569011, 45086801, were rated partially acceptable, and MRID 43679609 was rated acceptable based on today's scientific standards in a 11/12/2015 review for 2517-RTA (DP 427198), though all are currently supporting claims for 11556-128, 11556-125, 11556-127, 11556-130, and now 2517-RTA. As 2517-RTA contains the same amount of active ingredient that are proposed for this product, 83399-RT, these studies will not be re-reviewed and will be acceptable here.

IV. LABEL RECOMMENDATIONS:

(1) No changes to the Direction for Use section are suggested.

(2) The following marketing claims are acceptable:

- kills within 12 hours
- kills reinfesting fleas within 2 hours (note: *infesting* is not acceptable with the 2 hour timeframe)
- prevents flea infestation for 4 weeks [1 month][30 days]
- [brand name] is an effective flea adulticide, larvicide, and ovicide that kills [prevents] [treats][and][controls] against fleas
- Product is effective after exposure to sunlight, is water resistant, waterproof, and is still effective after bathing, or water immersion.
- Studies have shown that product kills fleas on dogs within 12 hours for up to 1 month [4 weeks][30 days] before adults start laying eggs
- To prevent [re]infestation, apply monthly
- Contains the active ingredient imidacloprid and the insect growth regulator, pyriproxyfen
- Contains the IGR that effectively kills eggs
- Protects against fleas [for up to 4 weeks][1 month][30 days]
- Treats [controls] and helps prevent further infestation
- Kills fleas in less than 24 hours
- Kills fleas before egg laying
- Kills fleas on dogs and puppies
- Kills fleas and their eggs
- Effectively kills eggs
- Disrupts [breaks] the flea life cycle
- Prevents fleas from developing into biting adults
- Kills [controls] flea life [cycles] [stages]
- Prevents eggs from hatching and developing into biting adults
- Kills larval stages of fleas
- Helps prevent recurring [re] infestations by killing adult fleas [within 12 hours], and continues to prevent [re]infestation for 1 month [4 weeks][30 days] (the 1 month time frame is mandatory here)
- Controls fleas for dogs and puppies
- [Treats] [controls] [prevents] flea infestation
- Provides flea protection [for 1 month][4 weeks][30 days]
- Controls against problematic fleas

- offers 3 way flea protection [kills][controls][prevents] adults, larvae, and eggs
- offers effective multistage control
- complete [comprehensive] and effective multistage flea control (note to PM: this has already been approved, but complete and comprehensive suggest heightened efficacy)
- formulated to target stages of flea development to treat and prevent flea development
- [kills] [treats][against] fleas which may serve as an intermediate host for tapeworm

The only reference to FAD should be written in the following manner: this product kills fleas that may cause FAD. (The label must indicate that the product kills the flea, not the corresponding condition).

(3) The following marketing claims are unacceptable:

- kills infesting fleas within 2 hours
- prevents flea infestation for *at least* 4 weeks [1 month][30 days]
- long lasting control
- effectively stops [ends] existing flea infestation
- kills reinfesting fleas before they can lay eggs
- treatment with product can reduce incidence of flea allergic dermatitis (FAD) or flea bite hypersensitivity (this must be superseded with *kills fleas that may cause*)
- regular monthly use kills fleas and aids in preventing [FAD][flea bite hypersensitivity][from developing]

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

September 25, 2015

MEMORANDUM

Subject:	Name of Pesticide Product:	IMIDACLOPRID AND PYRIPROXYFEN FOR DOGS
	EPA Reg. No. /File Symbol:	83399-RT
	DP Barcode:	DP 428210
	Decision No.:	503584
	Action Code:	R315
	E-Sub#:	--
	PC Code:	129099 (Imidacloprid: 9.1%) 129032 (Pyriproxyfen: 0.46%)
From:	Byron T. Backus, Ph.D., Toxicologist CITAB Registration Division (7505P)	Byron T. Backus Sept-25-2015
Through:	John Redden, M.S., Senior Risk Assessor CITAB Registration Division (7505P)	JCR
To:	Rita Kumar/Venus Eagle RM 01 IVB3 Registration Division (7505P)	
Registrant:	CEVA ANIMAL HEALTH, LLC 8735 Rosehill Road Lenexa, KS 66215	

FORMULATION FROM LABEL:

Active Ingredient(s):		by wt.
129099 Imidacloprid		9.10%
129032 Pyriproxyfen		0.46%
Other Ingredient(s):		90.44%
	TOTAL	100.00%

ACTION REQUESTED: The Risk Manager requests:

"CITAB/Companion Animal Team: Please provide a...full review of cited companion animal safety data to support registration of this dog spot-on product. This is an e-submission and all the information is in Documentum: Cover letter, data matrix, label, and CSF. Copies of the cover letter and proposed label dated 5/14/2015 are also attached..."

BACKGROUND: From the proposed label for EPA Reg. No. 83399-RT, doses are 0.4 mL (0.014 fl. oz.) for dogs weighing 3 to 10 lbs, 1.0 mL (0.034 fl. oz.) for dogs weighing 11-20 lbs, 2.5 mL (0.085 fl. oz.) for dogs weighing 21-55 lbs, and 4.0 mL (0.135 fl. oz.) for dogs weighing more than 55 lbs.

According to the data matrix (dated April 17, 2015) for EPA File Symbol 83399-RT the registrant has cited the following studies to satisfy the companion animal safety data requirements for this product: MRIDs 43679607, 43679608, 44099801, 44179801, 45097101, and 45097102.

PREVIOUS REVIEWS:

1. The study in MRID 43679607 was reviewed in HED (TXR 0011821, sign-off date 03/05/96) with the following summary:

   "Nine adult dogs of mixed breed (3 males, 6 females, one male and two females/group) were dermally exposed to Imidacloprid, 10% Spot-On. Dose levels were 50 mg/kg/day x 1 day, and 50 mg/kg/day x 3 days. Controls received placebo (formulation less active ingredient) at 50 mg/kg/day x 3 days.

   "No major treatment related dermal, clinical signs, body weight effects or clinical chemistry changes were observed. Necropsy was not done due to lack of toxicosis. The study demonstrates that adult dogs can tolerate up to 50 mg/kg without significant reactions.

   "This...study is classified as Acceptable when combined with another study, and satisfies the requirement for a domestic animal study in the dog, 18 lb (8 kg) body weight and above. The number of animals/group is too small and not in keeping with general study practice. However, when data are combined with the companion study in the dog (MRID 43679608), the information is considered useful."

2. The study in MRID 43679608 was reviewed in HED (TXR 0011821, sign-off date 03/05/96) with the following summary:

   "18 adult dogs of various breeds (3 males and 3 females/group) were dermally exposed to Imidacloprid, 10% Spot-On formulation at seven-day intervals for a total of eight treatments. Dose levels were 10 or 50 mg/kg. Controls received placebo (formulation less active ingredient) at 50 mg/kg.

   "No major treatment related dermal, clinical signs, body weight effects or clinical chemistry/hematology were observed. Necropsy was not done due to lack of toxicosis. The study demonstrates that adult dogs can tolerate up to 50 mg/kg of the active ingredient without significant reactions. Inadequate testing was done in dogs less than four months old.

"This repeated dose dermal study is classified as Acceptable and satisfies the requirements for a General Safety Evaluation for Topical Use (96-1) in the dog."

3. The study in MRID 44099801 was reviewed in HED (TXR 0012322, sign-off date 09/24/97) with the following summary:

   "In a domestic animal safety study (MRID #44099801), six 7 week-old puppies/sex were treated with Advantage™ (9.1% imidacloprid) at 5X the recommended use rate (2.0 mL if < 10 lbs; 5.0 mL if > 10 lbs) at weekly intervals for eight treatments. Six puppies/sex were treated with the vehicle control at the recommended use rate (0.4 mL if < 10 lbs; 1.0 mL if > 10 lbs) at weekly intervals for eight treatments. There was no evidence of treatment-related toxicity in clinical signs or clinical pathology parameters. All animals gained weight during the study. It was demonstrated that 7 week-old puppies can tolerate a dose of 5X the recommended use rate.

   "The study is considered acceptable and satisfies the draft guideline requirements (81-6) for a domestic animal safety study."

4. There is no record of a review for the study in MRID 44179801 [Shmidl, J.; Arther, R. (1996) Acute Oral Toxicity Evaluation of Imidacloprid (Advantage) in Dogs: Lab Project Number: TR-96D-010: 74764: J:USERS\LINDA\NOREPORT\JAS0171.RPT. Unpublished study prepared by Bayer Corp., Animal Health. 10 p.]. The following is a summary of that study:

   "The study was conducted to evaluate the acute toxicity of the formulation and the formulation minus the active ingredient (placebo) when administered orally at the topical use rate. The labeled use rate is 1.0 mL for dogs weighing 11 to 20 lb; 2.5 mL for 21 to 55 lb and 5.0 mL for dogs weighing > 55 lb. Group 1 dogs received a single treatment of placebo (formulation minus the active ingredient) equivalent to use rate volume. Group 2 dogs received a single treatment of the formulation at the use rate volume.

   "The treatment volumes were placed in gelatin capsules and administered directly in the throat area. The gelatin capsules were swallowed intact.

   "Two dogs in Group 2 vomited at approximately one hour following treatment. None of the remaining 10 dogs had any clinical signs."

   The purpose and protocol of this study are inconsistent with the 870.7200 Guidelines. This study, while providing relevant information, does not satisfy the 870.7200 data requirements.

5. The following is taken from the executive summary from the review (TXR 5001580, dated September 8, 2000) of the study in MRID 45097101 (beagle puppies, 7 weeks old at the time of the first treatment):

   "In a companion animal safety study (MRID 45097101), Advantage Plus® for Dogs (active ingredients: 9.1% imidacloprid w/w; 0.9% pyriproxyfen w/w) was applied topically at a dose of 2.0 mL/puppy (5X the label specified dose of 0.4 mL/puppy for puppies ≤ 10 lbs) to a group of 7 male and 7 female beagle puppies, seven weeks of age at the time of first treatment. Individual weights of the puppies in the treatment group ranged from 2.54 to 4.01 lbs (1.15-1.82 kg) on day

-1.. Controls (7M, 7F; weight range 2.49-5.03 lbs; 1.13-2.29 kg) were dosed with the vehicle alone at a dose of 2.0 mL/puppy (5.6X the volume of the vehicle present in the specified dose). Both groups were treated on study days 0, 7, 14, and 21. The recommended label dose is once a month. However, the labeling for these products includes the statement: "If re-treatment becomes necessary earlier than four weeks, do not re-treat more than once weekly."

"There were no deaths during the study. Following all treatments, a rough hair coat condition at the application site was noted on 3-14 puppies of both groups, and white powder was occasionally noted at the application sites; however, there were no signs of irritation...

"Despite the fact that the puppies may not have been entirely free of infection, and despite some deficiencies in the reporting of the data, the study is classified as **Acceptable** as a companion animal safety study (OPPTS 870.7200) in puppies. The lack of any indications of a consistent toxicological response following exposures (a total of 4) to 5X label-specified use applications of the test material indicates that an adequate safety margin exists for this formulation and its proposed use on puppies 7 weeks of age and older."

6. The following is taken from the executive summary from the review (TXR 5001580, dated September 8, 2000) of the study in MRID 45097102 (adult dogs):

"In a companion animal safety study (MRID 45097102) with adult beagles (ages ranging from 1 year and 3 months to 6 years), Advantage Plus® for Dogs (active ingredients: 9.1% Imidacloprid w/w; 0.9% Pyriproxyfen w/w) was applied topically at dose volumes of 5.0 mL for dogs weighing 11-20.4 lbs and 12.5 mL for dogs weighing 20.5-55 lbs (five times the recommended dose) to groups of 6 male and 6 female dogs... Controls were dosed with the vehicle at dose volumes of 5.0 mL for dogs weighing 11-20.4 lbs and 12.5 mL for dogs weighing 20.5-55 lbs (5.6 times the volume of the vehicle in the recommended dose)... Dogs were treated on study days 0, 7, 14, and 21.

"There were no deaths during the study. The dogs received no concomitant medication or therapy during the treatment period. The most prominent clinical sign was a rough appearance of the hair coats on dogs from both groups following treatment and lasting for up to 36 hours; however, there were no signs of irritation...

"The study is classified as **Acceptable/Guideline** as a companion animal safety study (OPPTS 870.7200) in dogs. The lack of any consistent indications of a toxicological response following exposures (a total of 4) to 5X label-specified use applications of the test material indicates that an adequate safety margin exists for this formulation and its proposed use on adult dogs."

7. In a TRB memorandum ("Minimum Treatment Weight and Age for EPA Reg. No. 11556-128") dated October 12, 2012 it was stated that:

"From data on pages 30 and 32 of MRID 45097101, the mean weight of the 7 males was 3.44 ± 0.39 lbs, while the mean weight of the 7 females was 3.06 ± 0.45 lbs. However, the 870.7200 Guidelines specify 6 animals/sex, so if the heaviest male and female are excluded, then the mean weight of the remaining 6 males was 3.34 ± 0.32 lbs, while the mean weight of the remaining 6 females was 2.92 ± 0.28 lbs (the mean weight of these 6 males and 6 females was 3.13 ± 0.36 lbs). **Based on these considerations, we can accept 3 lbs as the lowest minimum weight."**

"Individual puppy ages are reported on page 27 of MRID 45097101. The ages of the puppies on the day of first dosing ranged from 6 weeks and 5 days to 7 weeks and 0 days. **We can accept 7 weeks as the minimum age.**"

COMMENTS AND RECOMMENDATIONS:

1. After comparing the CSFs for 83399-RT and 11556-125, 11556-127, 11556-128 and 11556-130, CITAB concludes that these formulations are substantially similar, and that the companion animal safety studies that supported the registration of 11556-125 (and -127, -128, and -130) also support the registration of 83399-RT.

2. Based on the TRB reviews dated September 8, 2000 for 11556-125 and October 12, 2012 for 11556-128, CITAB concludes that the companion animal safety studies in MRIDs 45097101 and 45097102 (cited in the data matrix dated April 17, 2015) satisfy the 870.7200 data requirements to support the registration of 83399-RT for use on adult dogs and puppies 7 weeks of age and older, and support 3 pounds as the minimum weight (associated with a dose of 0.4 mL). The proposed doses and associated weight ranges [0.4 mL (0.014 fl. oz.) for dogs weighing 3 to 10 lbs, 1.0 mL (0.034 fl. oz.) for dogs weighing 11-20 lbs, 2.5 mL (0.085 fl. oz.) for dogs weighing 21-55 lbs, and 4.0 mL (0.135 fl. oz.) for dogs weighing more than 55 lbs] are acceptable.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

September 24, 2015

MEMORANDUM:

Subject:	Name of Pesticide Product:	IMIDACLOPRID & PYRIPROXYFEN SPOT-ON SOLUTION FOR DOGS
	EPA Reg. No. /File Symbol:	83399-RT
	DP Barcode:	DP 428209
	Decision No.:	503584
	Action Code:	R315
	PC Codes:	129099 (Imidacloprid: 9.1%) 129032 (Pyriproxyfen: 0.46%)
From:	Byron T. Backus, Ph.D., Toxicologist CITAB Registration Division (7505P)	Byron T. Backus Sept-24-2015
Through:	John Redden, M.S., Senior Risk Assessor CITAB Registration Division (7505P)	JCR
To:	Rita Kumar/Venus Eagle RM 01 IVB3 Registration Division (7505P)	
Registrant:	CEVA ANIMAL HEALTH, LLC	

FORMULATION FROM LABEL:

Active Ingredient(s):	by wt.
129099 Imidacloprid	9.10%
129032 Pyriproxyfen	0.46%
Other Ingredients:	90.44%
TOTAL	100.00%

ACTION REQUESTED: "Please provide a technical screen and full review of submitted and cited acute toxicity data to support registration of this dog spot-on product. This is an e-submission, and all the information is in Documentum: Cover letter, transmittal document, data matrix, CSF and label. Copies of the cover letter and proposed label dated 5/14/2015 are also attached…"

COMMENTS AND RECOMMENDATIONS:

1. To satisfy the acute toxicity data requirements, the registrant is citing (data matrix dated April 17, 2015) the following MRIDs: 49609007 (an unreviewed acute oral toxicity study dated April 10, 2015) and 49609008 (a primary eye irritation study in rabbits dated April 10, 2015), both submitted for EPA File Symbols 83399-RA and 83399-RT; 45096905 (an acute dermal toxicity study in rats); 45096906 (an acute inhalation toxicity study in rats); 45096908 (a primary dermal irritation study in rabbits; and 45096909 (a dermal sensitization study in guinea pigs; the last four cited studies were conducted on a formulation containing 9.1% Imidacloprid and 0.9% Pyriproxyfen, and were originally submitted to the Agency as supporting data for the Bayer products now registered under EPA Reg. Nos. 11556-125 through -130). These studies have been previously reviewed (TXR 5001579, dated August 30, 2000).

2. The registrant's cover letter dated April 17, 2015 includes the following:

   "This new end-use product contains two EPA registered active ingredients in the same amounts that have been combined in other EPA registered products – Advantage® II for Dogs, EPA Reg. Nos. 11556-128, -125, -127, and -130. Further, although this new end-use product is very similar to the EPA registered products Advantage II for Dogs, the formulation is somewhat different, as demonstrated by the acute oral toxicity of this new end-use product. The acute toxicity of this new end-use product does not meet any of the toxicity criteria specified in 40 CFR 157.22, and thus does not require Child Resistant Packaging."

3. The acute oral toxicity study in MRID 49609007 has been reviewed and classified as acceptable. Five rats were each dosed with 1.45 mL/kg of a test material having a specific gravity of 1.100; so that they were limit dosed at 1595 mg/kg. The first three rats that were dosed all survived; the fourth (dosed at 48 hours after the first three) died, while the fifth (dosed 48 hours after the fourth) survived. While there is no mention (or guidance) for a limit dose of 1600 (or 1595) mg/kg in either the OECD or OCSPP (OPPTS) Guidelines, the OECD guidance for 2000 mg/kg is: "Dose one animal at the test dose. If the animal dies, conduct the main test to determine the LD50." In this study the first rat that was dosed survived. From the results (1/5 died) there is an 81.25% probability that the test material has an $LD_{50} \geq 1595$ mg/kg, and the probability of an $LD_{50} \geq 1500$ mg/kg is greater than 81.25%. Based on these results it is concluded that 83399-RT is in Toxicity Category III for oral toxicity ($LD_{50} > 1595$ mg/kg) and does not require Child Resistant Packaging. It is noted that in previous testing (MRID 45096904) of a formulation containing 9.1% Imidacloprid and 0.9% Pyriproxyfen gave LD_{50} values of 1283 mg/kg for males (95% confidence limits were 680 to 1678 mg/kg) and 1000 mg/kg for females (95% confidence limits were incalculable).

4. The eye irritation study in MRID 49609008 has been reviewed and classified as acceptable. Since all three eyes were positive for conjunctival irritation at 48 hours (with 1/3 positive at 72 hours) and all eyes had complete cleared by day 7, the test material is in toxicity category III for eye irritation.

5. After a comparison of the CSFs for 83399-RT and 11556-125 it is concluded that the two formulations are toxicologically similar, so that the four cited studies (MRIDs 45096905, 45096906, 45096908 and 45096909) that were used to support 11556-125 will also support the

registration of 83399-RT. These studies were previously reviewed (TXR 5001579, August 30, 2000) and classified as acceptable.

6. All acute toxicity data requirements to support the registration of 83399-RT have been satisfied.

7. The following is the acute toxicity profile for 83399-RT, based on the results of the submitted and cited acute toxicity studies:

Acute oral LD_{50} (rat)	Tox. Category III	Acceptable	MRID 49609007
Acute dermal LD_{50} (rat)	Tox. Category IV	Cited	MRID 45096905
Acute inhalation LC_{50} (rat)	Tox. Category IV	Cited	MRID 45096906
Primary eye irritation (rabbit)	Tox. Category III	Acceptable	MRID 49609008
Primary dermal irritation (rabbit)	Tox. Category IV	Cited	MRID 45096908
Dermal sensitization (guinea pig)	Non-sensitizer	Cited	MRID 45096909

8. Based on the acute toxicity profile given above, the following is the precautionary and first aid labeling for 83399-RT, as obtained from the Label Review System:

PRODUCT ID #: **083399-00017**

PRODUCT NAME: **IMIDACLOPRID & PYRIPROXYFEN SPOT-ON SOLUTION FOR DOGS**

PRECAUTIONARY STATEMENTS

SIGNAL WORD: CAUTION

Hazards to Humans and Domestic Animals:

Harmful if swallowed. Causes moderate eye irritation. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Avoid contact with eyes or clothing.

First Aid:

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give anything to an unconscious person.

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

Reviewer: Byron T. Backus, Ph.D. **Date:** September 24, 2015
Risk Manager: Venus Eagle, RM 01

STUDY TYPE: Acute Oral Toxicity – CD®[Crl:CD®(SD)BR] Sprague-Dawley rats
OCSPP (OPPTS) 870.1100; OECD 425

TEST MATERIAL: Imidacloprid Pyriproxyfen Spot on Solution; Lot No. 150126-302-A; Expiration Date February 2016. Described (p. 11 of MRID 49609007) as a clear, pale yellow oily liquid with a specific gravity of 1.100 g/cc. The nominal concentrations of active ingredients were 9.1% (w/w) Imidacloprid and 0.46% (w/w) Pyriproxyfen. From information on p. 55 of MRID 49609007 the mean analytical concentrations were 9.146% Imidacloprid and 0.464% Pyriproxyfen.

SYNONYMS: Imidacloprid and Pyriproxyfen for Dogs

CITATION: Arulnesan, N. (2015) Acute Oral Toxicity Study of Imidacloprid Pyriproxyfen Spot On Solution in Sprague-Dawley Rats: Final Report. Project Number: 294722, PRO/294722 . Unpublished study prepared by Nucro-Technics. 55p. MRID 49609007.

SPONSOR: Provetis LLC
455 Sovereign Court
Ballwin, MO 63011, USA

SUBMITTER/DATA OWNER:
Ceva Animal Health, LLC

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 49609007), a total of 5 fasted (overnight) female Sprague-Dawley rats (source: Charles River Canada, Montreal, Quebec) were administered Imidacloprid Pyriproxyfen Spot On Solution at 1595 (1.45 mL/kg x 1100 mg/mL) mg/kg. The test material was administered undiluted by oral gavage using a feeding cannula inserted into the stomach.

The first 3 female rats were dosed at 1595 mg/kg. Since these 3 rats survived, the fourth animal was dosed 48 hours later and the last animal was dosed 48 hours after the fourth animal.

The fourth rat was found dead the day after dosing. Clinical signs for this rat included prostration and a mild convulsion at 23 minutes after dosing. At one hour post dosing, this rat was still prostrated. This rat showed neurological signs (paddling motions with the forelimbs, trembling, lateral recumbency) at 3-4 hours post-dosing.

The fifth rat had a wobbly gait and piloerection at approximately 45 minutes post-dose but had recovered and was normal at about 3 hours post-dose. No abnormal signs were seen in any of the other animals.

All surviving rats had weight gains in the period from day 1 to day 8 and again from day 8 to day 15.

The rat which was found dead on day 2 had a partially autolyzed stomach and partially autolyzed intestines. There were no abnormal findings in the rats which were sacrificed on day 15.

RESULTS and DISCUSSION:

A. **Mortality** – The fourth rat which was dosed was found dead the day after dosing. The other four rats survived.

B. **Clinical observations** – The rat which died had a mild convulsion and prostration at 23 minutes after dosing. At one hour post dosing, this rat was still prostrated. This rat showed neurological signs (paddling motions with the forelimbs, trembling, lateral recumbency) at 3-4 hours after dosing. The fifth rat had a wobbly gait and piloerection at approximately 45 minutes post-dose but had recovered and was normal at 3-4 hours post-dose.

C. **Gross Necropsy** – The rat which was found dead on day 2 had a partially autolyzed stomach and partially autolyzed intestines. There were no abnormal findings in the rats which were sacrificed on day 15.

D. **Reviewer's Conclusions** – This study is classified as acceptable and it satisfies the guideline requirements for an acute oral toxicity study (OCSPP [OPPTS] 870.1100; OECD 425). While there is no mention (or guidance) for a limit dose of 1600 (or 1595) mg/kg in either the OECD or OCSPP (OPPTS) Guidelines, the OECD guidance for 2000 mg/kg is: "Dose one animal at the test dose. If the animal dies, conduct the main test to determine the LD50." In this study the first rat that was dosed survived. From the results (1/5 died) there is an 81.25% probability that the test material has an $LD_{50} \geq 1595$ mg/kg (and the probability of an $LD_{50} \geq 1500$ mg/kg is even greater than 81.25%). Based on these results it is concluded that 83399-RT is in Toxicity Category III for oral toxicity ($LD_{50} > 1595$ mg/kg) and does not require Child Resistant Packaging.

Reviewer: Byron T. Backus, Ph.D. **Date:** September 24, 2015
Risk Manager: Venus Eagle, RM 01

STUDY TYPE: Primary Eye Irritation – New Zealand Albino Rabbits
OCSPP (OPPTS) 870.2400; OECD 404

TEST MATERIAL: Imidacloprid Pyriproxyfen Spot on Solution; Lot No. 150126-302-A; Expiration Date February 2016. Described (p. 9 of MRID 49609008) as a clear, pale yellow oily liquid with a specific gravity of 1.100 g/cc. The nominal concentrations of active ingredients were 9.1% (w/w) Imidacloprid and 0.46% (w/w) Pyriproxyfen. From information on p. 55 of MRID 49609007 the mean analytical concentrations (of this lot number) were 9.146% Imidacloprid and 0.464% Pyriproxyfen.

SYNONYMS: Imidacloprid and Pyriproxyfen for Dogs

CITATION: Mihalcea, E. (2015) Acute Eye Irritation Test of Imidacloprid / Pyriproxyfen Spot On Solution in New Zealand Albino Rabbits: Final Report. Project Number: 294739, PRO/294739. Unpublished study prepared by Nucro-Technics. 55p. MRID 49609008.

SPONSOR: Provetis LLC
455 Sovereign Court
Ballwin, MO 63011, USA

SUBMITTER/DATA OWNER:
Ceva Animal Health, LLC

EXECUTIVE SUMMARY: In an acute eye irritation study (MRID 49609008), 0.1 mL of test material was instilled in the conjunctival sac of one eye of each of 3 rabbits.

One rabbit was initially tested. As a severe or corrosive effect was not observed in this rabbit, 2 additional rabbits were tested.

There was no corneal opacity or iritis. All eyes were positive for conjunctival redness (grade 2) and chemosis (grade 2) at 24 hours; all eyes were positive for conjunctival redness (grade 2) at 48 hours, and 1/3 was positive for conjunctival redness (grade 2) at 72 hours. All scores were zero by day 7.

RESULTS and DISCUSSION:

A. **Eye irritation** – There was no corneal opacity or iritis. All eyes were positive for conjunctival redness (grade 2) and chemosis (grade 2) at 24 hours; all eyes were positive for conjunctival redness (grade 2) at 48 hours, and 1/3 was positive for conjunctival redness (grade 2) at 72 hours. All scores were zero by day 7.

B. **Reviewer's Conclusions** – This study is classified as acceptable and it satisfies the guideline requirements for an eye irritation study (OCSPP [OPPTS] 870.2400; OECD 404). Imidacloprid Pyriproxyfen Spot on Solution is in Toxicity Category III by this exposure route.

1. DP BARCODES: 428209				
2. PC CODES: 129099 (Imidacloprid); 129032 (Pyriproxyfen)				
3. CURRENT DATE: September 24, 2015				
4. TEST MATERIAL: Imidacloprid Pyriproxyfen Spot on Solution; Lot No. 150126-302-A; Expiration Date February 2016. Described (p. 9 of MRID 49609008) as a clear, pale yellow oily liquid with a specific gravity of 1.100 g/cc. The nominal concentrations of active ingredients were 9.1% (w/w) Imidacloprid and 0.46% (w/w) Pyriproxyfen. From information on p. 55 of MRID 49609007 the mean analytical concentrations (of this lot number) were 9.146% Imidacloprid and 0.464% Pyriproxyfen.				
Study/Species/Lab Study # /Date	**MRID**	**Results**	**Tox Cat**	**Core Grade**
Acute oral toxicity up-and-down (actually limit) test / rat / Nucro-Technics, Toronto, Ontario, Canada M1H2W4 / Laboratory Project No. 294722 / April 10, 2015 / OCSPP 870.1100; OECD 425	49609007	Fasted (overnight) female Sprague-Dawley rats were used. Test material was administered undiluted by oral gavage using a feeding cannula inserted into the stomach, with dosage at 1595 mg/kg (=1.45 mL/kg x 1100 mg/mL). The first 3 rats were dosed; since these all survived the 4th was dosed 48 hrs later and the 5th was dosed 48 hrs after the 4th. The 4th rat was found dead the day after dosing; clinical signs included prostration and a mild convulsion at 23 minutes after dosing. This rat showed neurological signs (paddling motions with the forelimbs, trembling, lateral recumbency) at 3-4 hrs after dosing. The 5th rat had a wobbly gait and piloerection at ~45 minutes post-dose but had recovered and was normal ~3 hrs after dosage. No abnormal signs were seen in the other animals. The rat found dead on day 2 had a partially autolyzed stomach and partially autolyzed intestines. There were no abnormal findings in the rats which were sacrificed on day 15. $LD_{50} \geq 1595$ mg/kg (probability 81.25%)	III	A
Primary eye irritation / rabbit / Nucro-Technics, Toronto, Ontario, Canada M1H2W4 / Laboratory Project No. 294739 / Care Products / Project Identification 11-14/06B / April 10, 2015 / OCSPP 870.2400; OECD 405	49609008	0.1 mL was instilled in the conjunctival sac of one eye of each of 3 rabbits. There was no corneal opacity or iritis. All eyes were positive for conjunctival redness (grade 2) and chemosis (grade 2) at 24 hrs; all were positive for conjunctival redness (grade 2) at 48 hrs, and 1/3 was positive for conjunctival redness at 72 hrs. All scores were zero on day 7.	III	A

Core Grade Key: A =Acceptable, S = Supplementary, W = Waived, U = Unacceptable, D = Data Gap

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
OFFICE OF PESTICIDE PROGRAMS REGISTRATION DIVISION (7505P)

FEE

~~DOCUMENT CONTAINS CONFIDENTIAL BUSINESS INFORMATION~~

DP BARCODE No.: 428208; **FILE SYMBOL No.**: 83399-RT; **PRODUCT NAME**: Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs; **DECISION No.**:503584; **PC Code(s)**: 129099, 129032; **ACTION CODE**: R315; **FOOD Use**: No

DATE OUT: October 13, 2015

SUBJECT: End Use Product Chemistry Review
Product Name: Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs

FROM: Shyam Mathur, Ph.D
Product Chemistry Team Leader
CITAB/RD (7505P)

10-13-15

TO: Rita Kumar / Venus Eagle, RM 01
I-V Branch-3 / RD (7505P)

Company Name: CEVA Animal Health, LLC
Formulation Type: Insecticide

INTRODUCTION:

The registrant has submitted an application for the registration of the new end use product "Imidacloprid & Pyriproxyfen Spot-On Solutions for Dogs". The registrant has submitted a CSF for basic formulation (dated 04-15-2015) and the supporting 830 series group A & group B product chemistry data with MRID Nos. 49609001 & 49609006 and the product label. On the advised of the Agency, the registrant has submitted a revised CSF for basic formulation dated (09-01-2015). CITAB has been asked to determine the acceptability of revised basic CSF and the supporting product chemistry data.

SUMMARY OF FINDINGS:

1. Name of Active Ingredient(s): Imidacloprid (9.1%) and Pyriproxyfen (0.46%)

2. Has the registrant claimed substantial similarity to a registered product?

[ ] Yes; [X] No; [ ] NA; if yes, give the registration number of the cited product.

3. All of the source materials of the active ingredient are derived from registered sources: [X] Yes [ ] No

4. All inert ingredients have been screened by IIAB and found to be approved for the proposed labeled Uses: [X] Yes; [ ] No

5. Confidential Statement of Formula(s):

[X] Proposed Basic - Dated: 04-15-2015; Re-submitted - Dated: 09-01-2015

[ ] Proposed Alternate – Dated:; Re-submitted – Dated:

Alternate CSF(s) complies with 40CFR§152.43: [ ] Yes; [ ] No; [X] NA

6. Product label

a. Ingredient statement: Nominal concentration of AI listed on CSF(s) concurs with product label

(PR Notice 91-2)

[X] Yes, if not, explain below:

Metallic equivalent:	[ ] Yes [X] NA;
Soluble arsenic:	[ ] Yes [X] NA
Isomeric ratios:	[ ] Yes [X] NA;
Acid equivalent:	[ ] Yes [X] NA; acid equivalent =

b. Health related sub statements: Product contains?

Petroleum distillate at > 10%:	[ ] Yes	[X] No	[ ] NA
Methanol at > 4%:	[ ] Yes	[X] No	[ ] NA
Sodium nitrite/sodium nitrate	[ ] Yes	[X] No	[ ] NA

c. Physical chemical hazard statement: Product label requires a statement per 40 CFR §156.78 for: flammability, explosive potential or electric insulator breakdown?
[ ] Yes [x] No

Is the sub statement in compliance with PR Notice 97-6? [ ] Yes, [x] NA; [ ] No; if not, explain Below:

d. Label requires an additional Storage and Disposal statement: [ ] Yes [X] No; if yes explain below:

7. Group **A**: Product Chemistry Data

Guideline No.	**Study Title**		**Data submitted**		**CITAB's Assessment of Data**	**MRID Nos.**
			Yes	**No**		
830.1550	Product Identity & Composition		X		A	49609001
830.1600	Description of materials used to produce the product		X		A	49609001
830.1650	Description of formulation process		X		A	49609001
830.1670	Discussion on the formation of impurities		X		A	49609001
830.1700	Preliminary analysis					
830.1750	Certified limits (158.350)	Standard certified limits	X		A	Revised Basic CSF (09-01-2015)
		Proposed Limits				
		Justification for wider limits				
830.1800	Enforcement analytical method		X		A	49609002 49609003

8. Group **B:**

Guideline No.	**Study Title**	**Value or Qualitative Description**	**CITABB's Assessment of Data**	**MRID Nos.**
830.6303	Physical State	Oily Liquid	A	49609004
830.6314	Oxidation/reduction	Not expected to be oxidized nor reduced based on the chemical structures of the constituents. Therefore this data requirement is not triggered.	A	49609004
830.6315	Flammability	104°C	A	49609006 49609004
830.6316	Explodability	Does not contain any ingredients that are considered explodable.	NA	49609004
830.7000	pH	Not dispersible in water	NA	49609005
830.7100	Viscosity	About 5.9 cSt at 20°C	A	49609005 49609004
830.7300	Bulk Density	1.1 g/ml @ 20°C	A	49609005 49609005
830.6317	Storage stability*	The study is in progress, the results will be submitted on completion.	I	49609004
830.6320	Corrosion characteristics*	The study is in progress and the results will be submitted on completion.	I	49609004

A = Acceptance, N = Not Acceptable, G = Data Gap, W = Waiver request, NA = Not applicable, I = In progress.

* The accelerated studies (2 weeks at 54°C) can be submitted in lieu for one year.

C. CONCLUSIONS:

The CITAB has reviewed the proposed revised basic CSF and the supporting product chemistry data and has concluded:

1. The proposed revised basic formulation CSF (dated 09-01-2015) is acceptable.

2. The product chemistry data submitted corresponding to the guideline 830 series group A and group B are acceptable

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

May 19, 2015

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

ALICIA HENK
CEVA ANIMAL HEALTH, LLC
8735 ROSEHILL ROAD
LENEXA, KS 66215-

PRODUCT NAME: Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs
COMPANY NAME: CEVA ANIMAL HEALTH, LLC
OPP IDENTIFICATION NUMBER:
EPA FILE SYMBOL: 83399-RT
EPA RECEIPT DATE: 05/18/15

SUBJECT: RECEIPT OF AMENDMENT

DEAR REGISTRANT:

The Office of Pesticide Programs has received your application for an amendment and it has passed an administrative screen for completeness.

During the initial screen we determined that the application appears to qualify for fast track review. The package will now be forwarded to the Product Manager for review to determine its acceptability for fast track status.

If you have any questions, please contact Registration Division, Risk Management Team 1, at (703) 308-8045.

Sincerely,

Front End Processing Staff
Information Services Branch
Information Technology & Resources Management Division

Fee for Service {968645K~

This package includes the following

- ◉ New Registration
- ○ Amendment

☐ Studies? ☐ Fee Waiver?

☐ volpay % Reduction: ___

for Division

- ○ AD
- ○ BPPD
- ◉ RD

Risk Mgr. 1

Receipt No. S- 968645

EPA File Symbol/Reg. No. 83399-RT

Pin-Punch Date: 5/18/2015

☑ This item is NOT subject to FFS action.

Action Code:

Requested:

Granted:

Amount Due: $ _____

Parent/Child Decisions:

☐ Inert Cleared for Intended Use ☐ Uncleared Inert in Product

Reviewer: Jennifer Gaines Date: 5/19/15

Remarks:

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060. Approval expires 05-31-98

EPA United States Environmental Protection Agency Washington, DC 20460

☒ Registration ☐ Amendment ☐ Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number: 83399-NEW
2. EPA Product Manager: Venus Eagle
3. Proposed Classification: ☒ None ☐ Restricted
4. Company/Product (Name): Ceva Animal Health, LLC/Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs
5. PM #1
5. Name and Address of Applicant (Include ZIP Code): Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215
☐ *Check if this is a new address*
6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:
EPA Reg. Nos. 11556-128, 11556-125, 11556-127, 11556-130
Product Name: Advantage II for dogs

Section II

☐ Amendment - Explain below.
☒ Resubmission in response to Agency letter dated 05-11-2015
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated XX-XX-XX
☐ "Me Too" Application
☒ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Ceva Animal Health, LLC is re-submitting a new product label for Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs in response to an Agency email from Rita Kumar on May 11, 2015.

Section III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging: ☐ Yes* ☒ No
***Certification must be submitted**

Unit Packaging: ☒ Yes ☐ No

If "Yes" Unit Packaging wgt.	No. per Container
0.014 fl oz (0.4 ml)	1,2,3,4,5,6,
0.034 fl oz (1.0 ml)	12, 24, 50,
0.085 fl oz (2.5 ml)	75, 100 vials
0.135 fl oz (4.0 ml)	

Water Soluble Packaging: ☐ Yes ☒ No

If "Yes" Package wgt.	No. per Container

2. Type of Container: ☐ Metal ☒ Plastic ☐ Glass ☐ Paper ☐ Other (Specify) Plastic Bag

3. Location of Net Contents Information: ☒ Label ☐ Container
4. Size(s) Retail Container: Various (see above)
5. Location of Label Directions: ☐ On Can ☒ On Labeling accompanying product
6. Manner in Which Label is Affixed to Product: ☐ Lithograph ☒ Other Printed box ☒ Paper glued ☐ Stenciled

Section IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Alicia Henk	Director, Development and Regulatory Affairs	(913) 754-7668

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received **(Stamped)**

2. Signature BY: Alicia Henk
3. Title: Director, Development and Regulatory Affairs
4. Typed Name: Alicia Henk
5. Date: May 14, 2015

*** Claimed confidential by submitter***

Screen

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460
OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
OFFICE OF PESTICIDE PROGRAMS REGISTRATION DIVISION (7505P)

DP BARCODE No.: D428208; **FILE SYMBOL No.**: 83399-RT (screen); **PRODUCT NAME**: Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs; **DECISION No.**: 503584; **PC Code(s)**: 129099, 129032; **ACTION CODE**: R315; **FOOD Use**: No

DATE OUT: July 27, 2015

SUBJECT: Completeness check screening for end use product "Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs"

FROM: Shyam Mathur,
Product Chemistry Team Leader
CITAB / RD (7505P)

SMathur 7-27-15

TO: Rita Kumar / Venus Eagle, RM 01
I-V Branch 3 / RD (7505P)

Company Name: CEVA Animal Health, LLC
Formulation Type: Insecticide
Active Ingredient(s): Imidacloprid (9.1%) and Pyriproxyfen (0.46%)
MRID Nos: 49609001 to 49609006

CONCLUSION:

Deficiencies: Yes
(if there are deficiencies they are indicated below each heading as Note 1, Note 2 Etc).

Group A: All required data submitted

Group B: All required data submitted

CSF: Basic CSF submitted (dated 04-15-2015)
Note 1: Basic CSF– Must be revised: In columns #11 of the CSF at least one name & address of the supplier for intentionally added inert ingredients must be listed. Alternate names & addresses of the suppliers must be provided on an attachment.

Note to PM: If the deficiencies are found in the screen results, please inform the registrant and bring back to author of this report the corrected deficiencies in response to 10 day letter, so that it can be attached to the original bean, if the data package is still in CITAB. New Bean is required in case the bean has been closed by CITAB. Thank you.

Kumar, Rita

From: Kumar, Rita
Sent: Monday, May 11, 2015 3:58 PM
To: Alicia Henk
Cc: Eagle, Venus
Subject: New dog and cat spot on applications 83399-RT and 83399-RA

Dear Alicia: I have not communicated with you in a while. Hope you are doing well and enjoying the spring weather.

I am doing a preliminary screen of these two spot-on applications, and have the following comments on the proposed labels:

1. Delete "[insert product name]", and add proposed product name on the front panel. This label must refer to the primary brand name.

2. Most of the brackets on the front panel statements and in optional marketing text are unnecessary or redundant, and make the label very confusing. Please simplify this label.

3. First Aid and Precautionary Statements are mandatory for both label and package insert. Delete the bracketed text from the two bulleted statements.

4. Delete the Optional text statement right below the two bulleted statements.

5. Delete the 3 optional text statements starting with: :Apply to cats.....". Only the sentence above with both minimum age and min weight are correct.

6. Delete brackets from the heading "[optional Marketing Text]".

7. The marketing text should be moved to end of the label. It should appear after the Precautionary statements and directions for use.

8. Delete "Fast Acting", or define it based on supporting efficacy data.

9. Under Directions for Use, the description of container (tube, via, applicator etc.) must match the picture. We suggest you use the term applicator, and delete other terms.

10. The statement regarding volume and pet weight needs to be clarified to reflect different volume and weight combination.

11. On the application form in column 6, indicate the product which was the basis of your proposed labeling and marketing text.

Please submit revised labels for further consideration of these applications. Since these are e-submissions, the revised labels must be uploaded to Documentum, therefore also be submitted on a CD thru front end with a hard copy of the cover letter explaining the changes, Please respond ASAP, so that the correct label can be sent for review. Thanks.

Regards,
Rita

Recd. 5/19/15

Completion of 21-Day Content Screen

pot-soton

PM- 1

EPA Reg. #(File Symbol) 83399 - RT

Decision # D_____

Data package delivered to you on 5/7/15 .
(date)

cket/Mini-jacket will be
ansferred to you today.
k up from Document Center)

Rita -
you already have this pkg.
This is just some of the front end-paper work
Thanks -
Terry

's 21–Day Content Team

83399 - RT
- RA

Memorandum

E-SUBMISSION

Date: 4 / 30 / 2015

To: _____, Regulatory Manager

From: Information Services Branch, ITRMD

Your receipt of this data submission is not an indication that MRIDs for the enclosed studies have been posted to OPPIN.

We expect that it will be approximately 5 days from the above date before the study-level data is available in OPPIN.

If you have any questions about this process, please contact Teresa Downs (305-5363).

This is a:
- ☒ fully accepted submission
- ☐ partially accepted submission
- ☐ rejected submission

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

April 22, 2015

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

CEVA ANIMAL HEALTH, LLC
8735 ROSEHILL ROAD
LENEXA, KS 66215

Report of Analysis for Compliance with PR Notice 11-03

Thank you for your submittal of 17-APR-15. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 11-03. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

Pages 107-108 Claimed confidential by submitter

TRANSMITTAL DOCUMENT

NAME AND ADDRESS OF SUBMITTER:
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

CONTACT PERSON (Return to)
Alicia Henk
Director, Pharmaceutical Development and Regulatory Affairs
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

REGULATORY ACTION SUPPORTED BY THIS PACKAGE:
This submission is prepared to support an EPA new product registration application for the new end-use product, Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs.

SUBMITTAL DATE:
April 17, 2015

Volume	Study Title	MRID No.
1	Administrative Materials	49609000
2	Group A Product Chemistry for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609001
3	Assay Determination of Imidacloprid and Pyriproxyfen in Imidacloprid 9.1% (w/w) and Pyriproxyfen 0.46% (w/w) Spot-On Solution	49609002
4	Assay Determination of Imidacloprid and Pyriproxyfen in Imidacloprid 9.1% (w/w) and Pyriproxyfen 0.46% (w/w) Spot-on Solution: Analytical Method Validation Report	49609003
5	Summary of Group B Product Chemistry and Waivers for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609004
6	Physical and Chemical Characteristics: Color, Physical State, Odor, Viscosity, and Density for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609005
7	Flashpoint for Ceva Animal Health's Imidacloprid Spot-On Solution, Imidacloprid & Pyriproxyfen Spot-On Solution, and Imidacloprid & Permethrin Spot-On Solution	49609006
8	Acute Oral Toxicity Study of Imidacloprid Pyriproxyfen Spot On Solution in Sprague-Dawley Rats	49609007
9	Acute Eye Irritation Test of Imidacloprid/Pyriproxyfen Spot On Solution in New Zealand Albino Rabbits	49609008

TRANSMITTAL DOCUMENT

NAME AND ADDRESS OF SUBMITTER:
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

CONTACT PERSON (Return to)
Alicia Henk
Director, Pharmaceutical Development and Regulatory Affairs
Ceva Animal Health, LLC
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Pages 111-112 Claimed confidential by submitter

21-Day Screen Completed by Contractor

21-Day Expires on 5-8-15

Jacket # 83399-RT
MRID# 496090

Content Screen: Recommend to Pass/Fail

11-3 Review: Pass/Fail/NA

Overall Status: Recommend to Pass/Fail

Transfer This Jacket to:

SHAUNTA HILL

PRIA 3 – 21 Day Content Screen Review Worksheet

(EPA/OPP Use Only)

September 2012

21 Day Screen Start Date: 4-17-15

Experts In-Processing Signature: B.B Date 4-22-15 Fee Paid: Yes ✓

Division management contacted on issues No_____ Yes_____ Date_____

EPA Reg. Number: 83399-RT	EPA Receipt Date: 4-17-15

	Items for Review	Yes	No	N/A*
1	**Application Form** (EPA Form 8570-1) signed & complete including package type	X		
2	**Confidential Statement of Formula** all boxes completed, form signed, and dated (EPA Form 8570-4)	X		
	a) All inerts, including fragrances, approved for the proposed uses (see Footnote A) non-food — yes: X; no:			
3	**Certification with Respect to Citation of Data** (EPA Form 8570-34) completed and signed (N/A if 100% repack)	X		
	Certificate and data matrix consistent	X		
	If applicant is relying on data that are compensable, is the offer to pay statement included. (see Footnote B) — yes: ; no:			
	If applicable, is there a letter of Authorization for exclusive use only.			
4	**Formulator's Exemption Statement** (EPA Form 8570-27) completed and signed (N/A if source is unregistered or applicant owns the technical)	X		
5	**Data Matrix** (EPA Form 8570-35) both internal and external copies (PR 98-5) completed and signed (N/A if 100% repack)	X		
	a) Selective Method (Fee category experts use) — yes: X; no:			
	b) Cite-All (Fee category experts use) — yes: ; no:			
	c) Applicant owns all data (Fee category experts use) — yes: ; no:			
6	**5 Copies of Label (Electronic labels on CD are encouraged and guidance is available)**	X		
7	**Is the data package consistent with PR Notice 86-5**	X		
8	**Notice of Filing included with petitions**			X

9	**If applicable for conventional applications, reduced risk rationale**			X
	Required Data and/or data waivers. See Footnote C.			
10	a) List study (or studies) not included with application			

Comments:

Documentation: Pass

Required forms are complete

Inerts: Pass

Approved for non-food use

II-3: Pass

MRID 496090 (e-sub)

MRID also associated w/ 8399-RA

Status: Pass

KC 4.30.2015

* N/A – Not Applicable

Footnotes

A. During the 21 day initial content review, all CSFs will be reviewed to determine whether all inerts listed, including fragrances, are approved for the proposed uses or have an application pending with the Agency. If an unapproved inert with no application pending with the Agency is identified, the applicant must either 1) resolve the inert issue by, for example, removing the inert, substituting it with an approved inert, submitting documentation that EPA approved the inert for the proposed pesticidal uses, correcting mistakes on the CSF, etc. or 2) provide the data to support OPP approval of the inert or 3) withdraw the application. Removing or substituting an inert ingredient will require a new CSF and may require submission of data. All information, forms, data and documentation resolving the inert issue must have been received by the Agency or the application withdrawn within the 21 day period, otherwise, the Agency will reject the application as described below.

To successfully complete this aspect of the 21 day initial content screen, applicants are **strongly encouraged** to verify that all inert ingredients have been approved for the application's uses or have an application pending with the Agency **even if a product is currently registered** by consulting the inert Web site and if the inert is not approved nor has an application pending with the Agency, to **obtain the necessary inert approval prior to submitting an application to register a pesticide product containing that inert ingredient.** Some inert ingredients are no longer approved for food uses or certain types of uses. The name and/or CAS number on a CSF must match the name and CAS number on this web site. Simple typographical errors in the name or CAS number have resulted in processing delays.

If an inert is not listed on the inert ingredient web site and the applicant believes that the inert has been approved, the applicant should contact the Inert Ingredient Assessment Branch (IIAB) at inertsbranch@epa.gov and resolve the issue. Copies of the correspondence with IIAB resolving the issue should accompany the application. All new inerts except PIP inerts are reviewed by IIAB. The IIAB should also be contacted for any questions on what supporting data needs to be submitted for and the Agency's inert review process. Questions on PIP inerts should be directed to the Chief of Microbial Pesticides Branch.

When a brand, trade, or proprietary name of an inert ingredient is listed on a CSF, additional information such as an alternate name of the inert, CAS number or other information must also be included to enable the Agency to determine if it has been approved. Each component of an inert mixture (including a fragrance) must be identified. In some cases, the supplier of the mixture or fragrance may need to provide this information to the Agency. Prior to the Agency's receipt of an application, applicants must arrange with a proprietary mixture or fragrance supplier to provide the component information to the Agency or promptly upon EPA's request. If the inert ingredients in a proprietary blend (including fragrances) cannot or are not identified or provided within the 21-day content review period, the Agency will reject the application.

During the 21 day content review, applicants should submit information to the individual identified by the Agency when the applicant is informed of an unapproved inert.

Unapproved Inerts Identified on CSFs

All applications except conventional new products and PIPs

Once an unapproved inert is identified on a CSF, the Agency will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Provide the required information necessary to identify an inert approval application that is pending with the Agency; or

3. Submit the information and data needed for the Agency to approve the unapproved inert. If this option is selected and implemented, the Agency may request an extension in the PRIA decision review timeframe to accommodate the inert review/approval process;

4. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of these options is selected and implemented by the applicant within the 21 day content review period, the Agency will reject the application and retain 25% of the full fee of the category identified.

Conventional New Product Applications

When the Registration Division identifies an unapproved inert on a CSF with an application for a new product that the applicant has not identified as requiring an inert approval (R300 or R301), it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert, including any required petition to establish or amend a tolerance or exemption from a tolerance. (This option may change the PRIA category for the application, which could require a longer decision review time and a larger fee. If additional fees are due, they must be received by the Agency within the 21 day content review period.)

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21-day content-review period, the Agency will reject the application and retain 25% of the appropriate fee for the new product-inert approval category.

PIP Applications

When the Biopesticide and Pollution Prevention Division identifies an unapproved inert on a PIP CSF and a request to approve the inert does not accompany the application, it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the spelling or name of the inert to that in 40 CFR 174, or providing documentation that the inert has been approved; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If an inert ingredient tolerance exemption petition is required, the petition must be received by the Agency and the B903 fee paid within the 21 day period. If this option is selected and implemented, the Agency will discuss harmonizing the timeframe for both actions.

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21 day content review period, the Agency will reject the application and retain 25% of the fee.

B. A policy on documentation of offers to pay is still being developed, however, for a me-too or fast track (similar/identical) new product, R300 or A530, an application without the necessary authorizations of offers to pay will be placed into either R301 or A531. The Agency recommends that authorizations of offers to pay be submitted with other PRIA applications to avoid delays in the Agency's decision.

C. Biopesticide applicants are advised to contact the Agency and discuss study waivers prior to submitting their application to the Agency. Documentation of such discussions should be submitted with the study waiver.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

April 21, 2015

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OPP Decision Number: D-503584
EPA File Symbol or Registration Number: 83399-RT
Product Name: Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs
EPA Receipt Date: 17-Apr-2015
EPA Company Number: 83399
Company Name: CEVA ANIMAL HEALTH, LLC

ALICIA HENK
CEVA ANIMAL HEALTH, LLC
8735 ROSEHILL ROAD
LENEXA, KS 66215-

SUBJECT: Receipt of Registration Application Subject to Registration Service Fee

Dear Registrant:

The Office of Pesticide Programs has received your application and certification of payment. If you submitted data with this application, the results of the PRN-2011-3 screen will be communicated separately. During the administrative screen, the Office of Pesticide Programs has determined that this Action is subject to a Pesticide Registration Service Fee as defined in the Pesticide Registration Improvement Act.

The Action has been identified as Action Code: R315

NEW END-USE NON-FOOD ANIMAL PRODUCT WITH SUBMISSION OF TWO OR MORE TARGET ANIMAL SAFETY STUDIES;INCLUDES DATA AND/OR WAIVERS OF DATA FOR ONLY:;PRODUCT CHEMISTRY;ACUTE TOXICITY;PUBLIC HEALTH PEST EFFICACY);ANIMAL SAFETY STUDIES;CHILD RESISTANT PACKAGING;

No additional payment is due at this time.

If you have any questions, please contact the Pesticide Registration Service Fee Ombudsman at (703) 347-8961.

Sincerely,
Teresa Downe
Front End Processing Staff
Information Technology & Resources Management Division

Fee for Service

{9672547~

This package includes the following

- ◉ New Registration
- ○ Amendment

☑ Studies? ☐ Fee Waiver?

☐ volpay % Reduction: ___

for Division

- ○ AD
- ○ BPPD
- ◉ RD

Risk Mgr. 1

Receipt No. S- 967254

EPA File Symbol/Reg. No. 83399-RT

Pin-Punch Date: 4/17/2015

☐ This item is NOT subject to FFS action.

Action Code:

Requested: R315

Granted: R315

Amount Due: $ 8,402

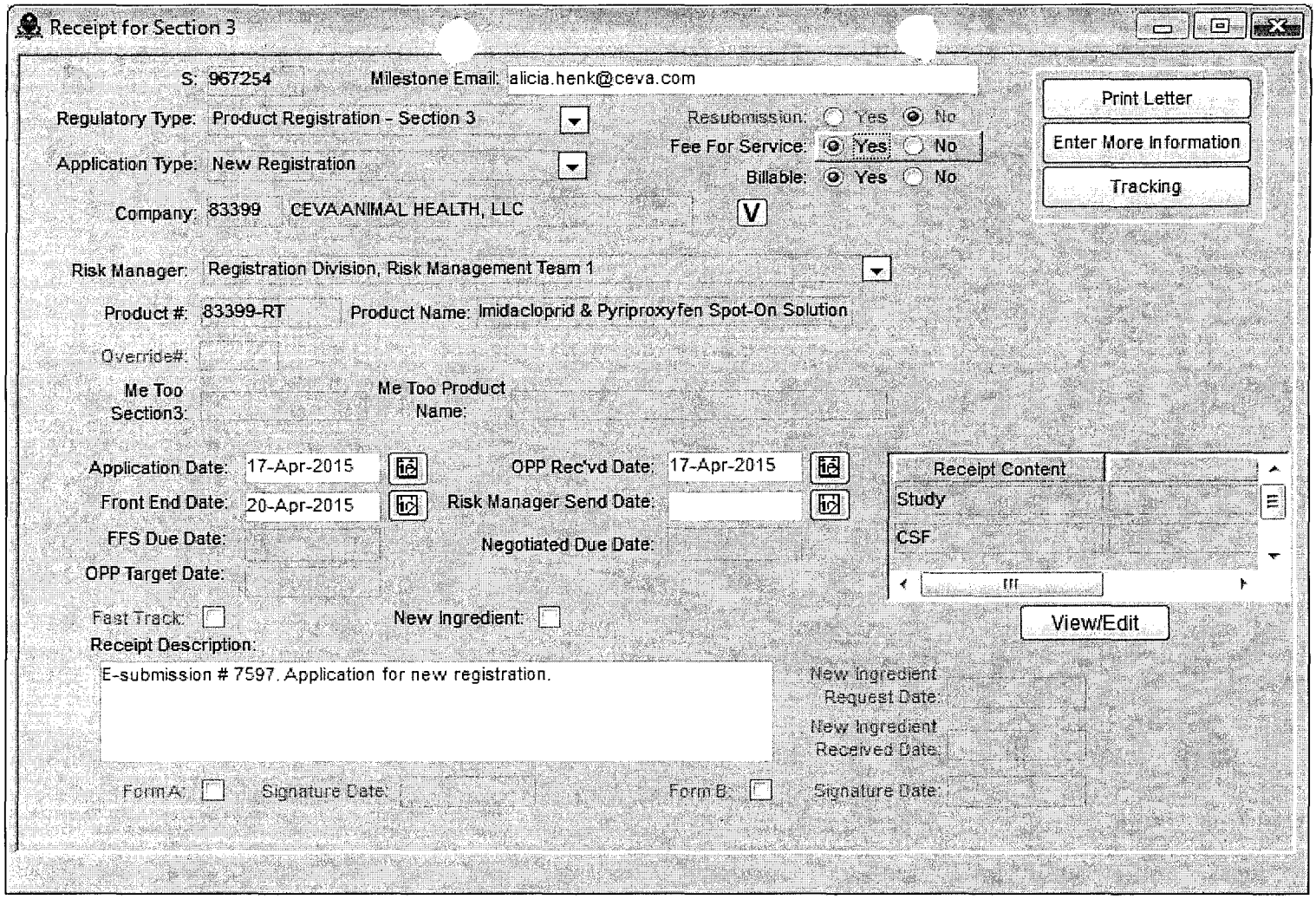
Parent/Child Decisions:

☐ Inert Cleared for Intended Use ☐ Uncleared Inert in Product

Reviewer: Jennifer Gaines Date: 4/21/15

Remarks:

e-Submission


Receipt for Section 3
S: 967254
Milestone Email: alicia.henk@ceva.com
Regulatory Type: Product Registration - Section 3
Application Type: New Registration
Company: 83399 CEVAANIMAL HEALTH, LLC
Resubmission: Yes No
Fee For Service: Yes No
Billable: Yes No
Print Letter
Enter More Information
Tracking
Risk Manager: Registration Division, Risk Management Team 1
Product #: 83399-RT
Product Name: Imidacloprid & Pyriproxyfen Spot-On Solution
Override#:
Me Too Section3:
Me Too Product Name:
Application Date: 17-Apr-2015
OPP Rec'vd Date: 17-Apr-2015
Front End Date: 20-Apr-2015
Risk Manager Send Date:
FFS Due Date:
Negotiated Due Date:
OPP Target Date:
Receipt Content
Study
CSF
View/Edit
Fast Track:
New Ingredient:
Receipt Description:
E-submission # 7597. Application for new registration.
New Ingredient Request Date:
New Ingredient Received Date:
FormA:
Signature Date:
Form B:
Signature Date:

Pay.gov

Receipt

Your payment is complete

Pay.gov Tracking ID: 25KRJCHF
Agency Tracking ID: 74788230168
Form Name: Pesticide Registration Improvement Act - Prepayment
Application Name: PRIA Service Fees

Payment Information

Payment Type: Debit or credit card
Payment Amount: $8,400.00
Transaction Date: 04/16/2015 09:04:47 AM EDT
Payment Date: 04/16/2015
Registration Number:
Company Name: Ceva Animal Health, LLC
Company Number: 83399
Action Code: R315

Account Information

Card Holder Name: Tracey Bailes
Billing Address: 8735 Rosehill Rd
Billing Address 2: Suite 300
City: Lenexa
Country: United States
State/Province: KS
ZIP/Postal Code: 66215
Card Type: American Express
Card Number: **********2019

Email Confirmation Receipt

Confirmation Receipts have been emailed to:
katy.hernandez@ceva.com
alicia.henk@ceva.com

e-Submission

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060. Approval expires 05-31-98

EPA United States **Environmental Protection Agency** Washington, DC 20460

☒ **Registration** ☐ **Amendment** ☐ **Other**

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number: 83399-NEW
2. EPA Product Manager: Venus Eagle
3. Proposed Classification: ☒ None ☐ Restricted
4. Company/Product (Name): Ceva Animal Health, LLC/Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs
5. PM #1
5. Name and Address of Applicant (Include ZIP Code):

Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

☐ *Check if this is a new address*

6. **Expedited Review**. In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:

EPA Reg. Nos. _____

Product Name _____

Section II

☐ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated XX-XX-XX
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated XX-XX-XX
☐ "Me Too" Application
☒ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Ceva Animal Health, LLC is submitting a new product registration application for Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs. Ceva Animal Health, LLC requests that the Agency review the end-use product registration as a 9 month PRIA timeframe under R315.

Section III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging: ☐ Yes* ☒ No

***Certification must be submitted**

Unit Packaging: ☒ Yes ☐ No

If "Yes" Unit Packaging wgt.	No. per Container
0.014 fl oz (0.4 ml)	1,2,3,4,5,6,
0.034 fl oz (1.0 ml)	12, 24, 50,
0.085 fl oz (2.5 ml)	75, 100 vials
0.135 fl oz (4.0 ml)	

Water Soluble Packaging: ☐ Yes ☒ No

If "Yes" Package wgt.	No. per Container

2. Type of Container: ☐ Metal ☒ Plastic ☐ Glass ☐ Paper ☐ Other (Specify) Plastic Bag

3. Location of Net Contents Information: ☒ Label ☐ Container

4. Size(s) Retail Container: Various (see above)

5. Location of Label Directions: ☐ On Can ☒ On Labeling accompanying product

6. Manner in Which Label is Affixed to Product: ☐ Lithograph ☒ Paper glued ☐ Stenciled ☒ Other Printed box

Section IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Alicia Henk	Director, Pharmaceutical Development and Regulatory Affairs	(913) 754-7668

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received **(Stamped)**

2. Signature BY: Alicia Henk

3. Title: Director, Pharmaceutical Development and Regulatory Affairs

4. Typed Name: Alicia Henk

5. Date: April 17, 2015

e-Submission

Claimed confidential by submitter

TRANSMITTAL DOCUMENT

NAME AND ADDRESS OF SUBMITTER:
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

CONTACT PERSON (Return to)
Alicia Henk
Director, Pharmaceutical Development and Regulatory Affairs
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

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Form approved. OMB No. 2070-0060, 2070-0057, 70-0107, 2070-0122, 2070-0164.

EPA

United States
Environmental Protection Agency
Washington, DC 20460

Formulator's Exemption Statement

(40 CFR 152.85)

Applicant's Name and Address	EPA File Symbol/Registration Number
Ceva Animal Health, LLC 8735 Rosehill Road Lenexa, KS 66215	83399-NEW
	Product Name Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs
	Date of Confidential Statement of Formula *(EPA Form 8570-4)* 04/15/2015

As an authorized representative of the applicant for registration of the product identified above, I certify that:

(1) This product contains the following active ingredient(s):

Imidacloprid
Pyriproxyfen

(2) Of these, each active ingredient listed in paragraph (4) is present solely as the result of the use of that active ingredient in the manufacturing, formulation or repackaging another product which contains that active ingredient which is registered under FIFRA Section 3, is purchased by us from another person and meets the requirements of 40 CFR section 158.50(e)(2) or (3).

(3) Indicate by checking (A) or (B) below which paragraph applies:

☑ (A) An accurate Confidential Statement of Formula *(EPA FORM 8570-4)* for the above identified product is attached to this statement. That formula statement indicates, by company name, registration number, and product name, the source of the active ingredient(s) listed in paragraph (1).

OR

☐ (B) The Confidential Statement of Formula (CSF)(EPA Form 8570-4) referenced above and on file with the EPA is complete, current, an accurate and contains the information required on the current CSF.

(4) The following active ingredients in this product qualify for the formulator's exemption.

Source

Active Ingredient	Product Name	Registration Number
Imidacloprid Pyriproxyfen	[redacted]	

Signature	Name and Title	Date
Alicia Henk	Alicia Henk Director, Development & Regulatory Affairs	04/17/2015

EPA Form 8570-27 (Rev. 06-2004)

Copy 1 – EPA
Copy 2 - Applicant copy

e-Submission

Product ingredient source information may be entitled to confidential treatment

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
1200 Pennsylvania Avenue, N.W.
WASHINGTON, D.C. 20460

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215	EPA Registration Number/File Symbol 83399-NEW
Active Ingredient(s) and/or representative test compound(s) Imidacloprid, Pyriproxyfen	Date 04/17/2015
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) Indoor non-food	Product Name Imidacloprid & Pyriproxyfen Spot-On Solution for Do

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

☑ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses .

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (I) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
	04/17/2015	Alicia Henk, Director, Development & Reg. Affairs

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

Date: April 17, 2015 | **EPA Reg No./File Symbol:** 83399-NEW | Page 1 of 3

Applicant's/Registrant's Name & Address
Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215

Product:
Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs

Ingredients: Imidacloprid, Pyriproxyfen

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Product Chemistry					
830.1550, 830.1600, 830.1620, 830.1650, 830.1670, 830.1750	Group A Product Chemistry for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609001	Ceva Animal Health, LLC	OWN	
830.1800	Assay Determination of Imidacloprid and Pyriproxyfen in Imidacloprid 9.1% (w/w) and Pyriproxyfen 0.46% (w/w) Spot-On Solution	49609002	Ceva Animal Health, LLC	OWN	
830.1800	Assay Determination of Imidacloprid and Pyriproxyfen in Imidacloprid 9.1% (w/w) and Pyriproxyfen 0.46% (w/w) Spot-On Solution: Analytical Method Validation Report	49609003	Ceva Animal Health, LLC	OWN	
830.6302, 830.6303, 830.6304, 830.6313, 830.6314, 830.6315, 830.6316, 830.6319, 830.6321, 830.7000, 830.7100, 830.7300. 830.7520	Summary of Group B Product Chemistry and Waivers for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609004	Ceva Animal Health, LLC	OWN	
830.6302, 830.6303, 830.6304, 830.7100, 830.7300	Physical and Chemical Characteristics: Color, Physical State, Odor, Viscosity, and Density for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609005	Ceva Animal Health, LLC	OWN	
830.6315	Flashpoint for Ceva Animal Health's Imidacloprid Spot-On Solution, Imidacloprid & Pyriproxyfen Spot-On Solution, and Imidacloprid & Permethrin Spot-On Solution	49609006	Ceva Animal Health, LLC	OWN	
Toxicology Data Requirements					
870.1100	Acute Oral Toxicity Study of Imidacloprid Pyriproxyfen Spot On Solution in Sprague-Dawley Rats	49609007	Ceva Animal Health, LLC	OWN	
870.1200	Acute Dermal Toxicity Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096905	Bayer Animal Health	OLD	
870.1300	Acute Four-Hour Inhalation Toxicity Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096906	Bayer Animal Health	OLD	
870.2400	Acute Eye Irritation Test of Imidacloprid/Pyriproxyfen Spot On Solution in New Zealand Albino Rabbits	49609008	Ceva Animal Health, LLC	OWN	
870.2500	Primary Dermal Irritation Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096908	Bayer Animal Health	OLD	

Signature	**Name and Title**	**Date**
	Alicia Henk, Director Pharmaceutical Development and Regulatory Affairs, Ceva Animal Health, LLC	April 17, 2015

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
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DATA MATRIX

Date: April 17, 2015		**EPA Reg No./File Symbol:** 83399-NEW	Page 2 of 3
Applicant's/Registrant's Name & Address Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215		**Product:** Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs	
Ingredients: Imidacloprid, Pyriproxyfen			

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.2600	Dermal Sensitization Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096909	Bayer Animal Health	OLD	
870.7200	Evaluation of the General Safety of 9.1% Imidacloprid with 0.9% Pyriproxyfen Spot On Formulation in the Target Species, Seven Week Old Puppies	45097101	Bayer Animal Health	OLD	
870.7200	Evaluation of the General Safety of 9.1% Imidacloprid with 0.9% Pyriproxyfen Spot On Formulation in the Target Species, Adult Dogs	45097102	Bayer Animal Health	OLD	
870.7200	Acute Toxicity Evaluation for Dermal Treatment of Dogs with Imidacloprid (Bay t 7391) Spot-on: Lab Project Number: 74580: TR-94D-010. Unpublished study prepared by Miles Inc. 19 p.	43679607	Bayer Animal Health	OLD	
870.7200	General Safety Evaluation for Topical Use of Imidacloprid (Bay t 7391) Spot-On On Dogs: Lab Project Number: 74590: TR-95D-005. Unpublished study prepared by Bayer Corp. 40 p.	43679608	Bayer Animal Health	OLD	
870.7200	General Safety Evaluation for Topical Use of Imidacloprid (Advantage) Spot-On on Puppies: Lab Project Number: TR-96D-003: 74730: 10332. Unpublished study prepared by Bayer Corp. 47 p.	44099801	Bayer Animal Health	OLD	
870.7200	Acute Oral Toxicity Evaluation of Imidacloprid (Advantage) in Dogs: Lab Project Number: TR-96D-010: 74764: J:USERS\LINDA\NOREPORT\JAS0171.RPT. Unpublished study prepared by Bayer Corp., Animal Health. 10 p.	44179801	Bayer Animal Health	OLD	
Product Performance Test Guidelines					
810.3300	Efficacy Evaluation of Bay t 7391 (Imidacloprid) 10% Solution Applied Dermally for Control of Fleas on Dogs	43679609	Bayer Animal Health	OLD	
810.3300	Efficacy Confirmation of NTN 33893 (Imidacloprid) Solution Applied Dermally for Control of Fleas on Dogs	43679610	Bayer Animal Health	OLD	

Signature	**Name and Title**	**Date**
Alicia Henk	Alicia Henk, Director Pharmaceutical Development and Regulatory Affairs, Ceva Animal Health, LLC	April 17, 2015

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

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DATA MATRIX

Date: April 17, 2015 | **EPA Reg No./File Symbol:** 83399-NEW | Page 3 of 3

Applicant's/Registrant's Name & Address
Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215

Product:
Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs

Ingredients: Imidacloprid, Pyriproxyfen

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Comparative Evaluation of How Quickly Advantage and Frontline (Fipronil) Top Spot Kill Fleas on Dogs: (Final Report)	44256901	Bayer Animal Health	OLD	
810.3300	Imidacloprid Topical Formulation: Larvicidal Effect Against Ctenocephalides felis in the Surroundings of Treated Dogs	44256902	Bayer Animal Health	OLD	
810.3300	Evaluation of the Effects of Shampooing or Water Immersion on the Initial and Residual Efficacy of Advantage for Flea Control on Dogs	44256903	Bayer Animal Health	OLD	
810.3300	Nylar 50 (percent) Concentrate: Product Performance/Efficacy Reports. Unpublished study prepared by McLaughlin Gormley King. 79 p.	45086801	McLaughlin Gormley King Company	OLD	

Signature	Name and Title	Date
Alicia Henk	Alicia Henk, Director Pharmaceutical Development and Regulatory Affairs, Ceva Animal Health, LLC	April 17, 2015

Ceva Animal Health, LLC

[FRONT PANEL]

[Ceva] [Imidacloprid and Pyriproxyfen] [insert product name] for Dogs

[Prevents and Treats Flea and Lice Infestation on Dogs [and puppies 7 weeks and older]]
[Aids in the Prevention and Treatment of Flea and Lice Infestation on Dogs [and puppies 7 weeks and older]]
[[Name of Product] Treats and Prevents Flea and Lice Infestations on Dogs [and puppies 7 weeks and older]]

Alternate Brand Names include: [Brand Name for Dogs [and Puppies]]

Picture of dog/puppy according to weight range

ACTIVE INGREDIENTS:	
Imidacloprid	9.10%
Pyriproxyfen	0.46%
OTHER INGREDIENTS:	90.44%
TOTAL	100.00%

NET CONTENTS: **XXX fl oz (XXX mL)**
[XX Doses [each dose XXX fl oz]]

EPA Est. No. TBD **EPA Reg. No. 83399—NEW**

["Do Not Use on Cats" icon, icon size 1.5cm x 1.5cm on final or larger as indicated]

[FRONT PANEL]

KEEP OUT OF REACH OF CHILDREN

CAUTION

- See Back Panel [or] [Package Insert] for First Aid and Precautionary Statements
- See [[Back] [or] [Side] [Label] [Panel][or] [Package Insert]for Directions for Use and Storage and Disposal Instructions

[Optional text appears in brackets/parenthesis – the final label may include some or all of the optional text on front, back or side label panels or package insert]

[For Use Only on Dogs [and puppies] 7 weeks of age or older [and weighing over 3 lbs]]
[Only for Dogs [and puppies] 7 weeks of age or older and over 3 lbs]
[Use on Dogs [and puppies] 7 weeks of age or older [and weighing over 3 lbs]]

[Optional Marketing Claims]

[Fleas]
[[Brand Name] contains the active ingredient [imidacloprid],[and an/the] [insect growth regulator][IGR] pyriproxyfen]
[[Brand Name] contains an [insect growth regulator [IGR] that effectively kills flea eggs]]
[[Brand Name] prevents flea infestation for at least [four] [4] weeks] [1 month] [30 days]
[[Brand Name] prevents flea infestation for up to [four] [4] weeks] [1 month] [30 days]

Information in [ ] is optional

[Protects against fleas [for up to [four] [4] weeks]] [1 month] [30 days]
[[Brand Name] helps prevent further flea infestation for up to [four] [4] weeks]] [1 month] [30 days]
[[Brand Name] [continually] works to prevent flea infestation for up to [four] [4] weeks]] [1 month] [30 days]
[[Effectively] [stops] [ends] [controls] existing flea infestation by killing adult fleas] [and prevents further infestation] [in the home]
[[Brand Name] treats, controls, and prevents flea infestation]
[[Brand Name] treats for fleas [within 12 hours] on dogs]
[Kills fleas within [in] [12] [twelve] hours [after application]]
[Kills fleas in less than 24 hours]
[Kills fleas before egg laying]
[Kills fleas before eggs can be laid]
[Kills fleas on dogs and puppies]
[Kills [re]infesting fleas within 2 hours]
[Kills fleas and their eggs]
[Effectively kills flea eggs]

[[Effectively] Disrupts the flea cycle and kills larval flea stage]
[Breaks the flea life cycle [and] [prevents] [stops] flea eggs [and larvae] from developing into adult [biting] fleas]
[Kills flea eggs from hatching [and] [developing into biting adults]]

[[Kills] [and] [controls] fleas at all life stages]
[Larval flea stages are killed after [Brand Name] is applied to dog]
[Kills flea larval stage after contact [treatment] with [Brand name]]
[Larval flea stages are killed after contact with [Brand Name] treated dog]

[Prevents [re]infestation by killing adult fleas before [they] [lay eggs] [egg laying] [eggs can be laid]]
[Kills reinfesting fleas within 2 hours] [and] [protects against further flea infestation [up to [four] [4] [weeks] [a month] [30 days]]]
[Prevents [recurring] [re]infestation[s] by killing adult fleas [within 12 hours] [and continues to prevent [re] [infestations] for up to [four] [4] [weeks] [a month] [30 days]]]

[Controls fleas for dogs and puppies [7weeks or older]]
[Treats flea infestation [on dogs [and puppies] 7 weeks or older]]]
[Provides flea protection [up to [four] [4] [weeks] [a month] [30 days]]
[Controls against [problematic] [irritating] [annoying] flea[s] bites]
[Treatment with [Brand Name] can reduce incidences of flea allergic dermatitis (FAD) or flea bit hypersensitivity [by killing fleas on contact]]
[[Brand Name] [offers 3-way flea protection] that [kills] [controls] [prevents] against adults, larvae, and eggs]
[[An effective] flea adulticide, larvicide, and ovicide [that [kills][prevents][,treats] [,and] [controls] against fleas]]
[[Brand Name] offers effective multistage flea control]

[Complete and effective [once a month] [flea] [protection] [prevention and treatment]]
[Comprehensive and effective flea treatment [for your dog]]
[Regular monthly use of [Brand Name] kills fleas and aids in preventing flea allergy dermatitis] [flea bit hypersensitivity] [from developing]]
[Monthly topical treatment of [Brand name] kills fleas and treats flea infestation [for dogs [and puppies 7 weeks or older]]]

[[[Specially] Formulated to] target[s] every stage of flea development [to treat and prevent flea

Information in [ ] is optional

infestation]]

[[Brand Name] treats for fleas [in 12 hours] on dogs and puppies [7 weeks or older]]
[Monthly treatment prevents and treats flea on dogs 7 weeks or older]

[[Kills] [Treats] [against] fleas which may serve as intermediate hosts for tapeworm]

[Multiple Infestations]
[[Brand Name] treats [prevents] [and] [controls] against flea and lice infestation]
[Effectively treats flea and lice [infestation]]
[[Brand Name] [offers] dual protection against fleas and [biting] [chewing] lice]

[All Others]
[For Dogs and puppies 7 weeks or older]
[For Use on puppies 7 weeks or older]
[For Use on Dogs Only]
[Do Not Use on Cats]
[Easy to Use [Applicator]]
[Easy to Apply [Applicator]]
[Applies Easily]
[Fast Acting]
[[Brand Name] recommends monthly treatments]
[Easy One Step Flea and Lice Prevention for up to [four] [4] weeks] [a month][30 days]
[For Best Results Apply [Monthly] [30 Days] [every [4] [four] weeks]]
[Best used year round] [once [a month] [every] [four] [4] [weeks] [30 days]]
[Use [Monthly] [Every [30 Days] [4] [Four] Weeks]] for Best Results]
[Only One Treatment Needed [Every [Month] [30 Days] [[4] [Four] Weeks]]]
[One treatment remains effective for [4] [four] [weeks] [1 month] [30days]]
[Convenient]
[Water-Resistant After Application]
[[Brand Name] is waterproof after application]
[Brand Name] [is effective after [bathing] [shampooing]]
[[Brand Name] Effective [even] after exposure to rain or sunlight]
[Specially formulated for fast acting [and long lasting] control of fleas for [1 month] [4 weeks] on dogs]
[Contains the [exact] [same] active ingredients in [Bayer] [Advantage II] [for dogs]]
[Compare to [Bayer] Advantage II] for dogs]
[Brand Name] is not manufactured or distributed by Bayer [Animal Health]

Information in [ ] is optional

Ceva Animal Health, LLC

BACK PANEL

READ ENTIRE LABEL BEFORE EACH USE
USE ONLY ON DOGS

IMPORTANT CONSUMER INFORMATION

[[PRODUCT NAME] [Brand name] [This product] kills fleas [within] [12] hours]. **[PRODUCT NAME]** [Brand name] prevents flea infestation for at least [[4] [four] weeks] [and [treats] [1 month] [30 days]]. [The active ingredient in [Brand name] [this product] is formulated for fast acting [and long lasting] control of fleas for [1 month] [4 weeks] [30days] on dogs.]

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS

CAUTION: Harmful if swallowed. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash hands thoroughly with soap and warm water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Keep out of reach of children.

HAZARDS TO DOMESTIC ANIMALS

FOR EXTERNAL USE ON DOGS ONLY. Do not use on puppies under 7 weeks of age or puppies weighing less than 3 lbs. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing dogs. Individual sensitivities, while rare, may occur after using ANY pesticide product for pets. If signs persist, or become more severe, consult a veterinarian immediately or call us at 1-800-999-0297. If your dog is on medication, consult your veterinarian before using this or any other product. DO NOT USE ON CATS.

FIRST AID	
IF IN EYES:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
IF SWALLOWED:	• Call a poison control center or doctor immediately for treatment advice. • Have a person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything by mouth to an unconscious person.
IF ON SKIN	• Wash with plenty of soap and water.
HOT LINE NUMBER	
Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may contact 1-800-999-0297 weekdays between 9am and 6pm EST or 1-888-426-4435 for emergency medical treatment information.	

RESTRICTIONS. For use only on dogs [and puppies] 7 weeks and older. Do not use on other animals. Do not apply to dogs or puppies weighing less than 3 lbs. Do not apply more than [one][1] tube per treatment. Do not have contact or allow children to have contact with treated area until completely dry.

Information in [ ] is optional

Ceva Animal Health, LLC

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

DO NOT ALLOW CHILDREN TO APPLY PRODUCT. TO PREVENT HARM TO YOU AND YOUR DOG, READ ENTIRE LABEL BEFORE EACH USE. FOLLOW ALL DIRECTIONS AND PRECAUTIONARY STATEMENTS CAREFULLY. FOR EXTERNAL USE ON DOGS ONLY. DO NOT USE ON OTHER ANIMALS.

DO NOT USE ON CATS. Do not use on puppies under 7 weeks of age or weighing less than 3lbs. Weigh your dog to be sure you are applying the right dose formulated for the weight of your dog. Do not treat your dog with more than one pesticide product at a time. Over dosing your dog can result in serious illness and even death. **Best if used year round.** Certain medications can interact with pesticides. Consult a veterinarian before using this product on debilitated, aged, medicated, pregnant, or nursing dogs. Consult a veterinarian before using on dogs with known organ dysfunction. If your dog is exhibiting signs of and/or are being treated for skin dermatitis, talk to your vet before applying any topical flea and tick control product.

Sensitivities may occur after using ANY pesticide product on dogs. Dogs may experience some temporary irritation at the site of product application. If signs of sensitivity occur, bathe your dog with a mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately by calling 1-888-426-4435.

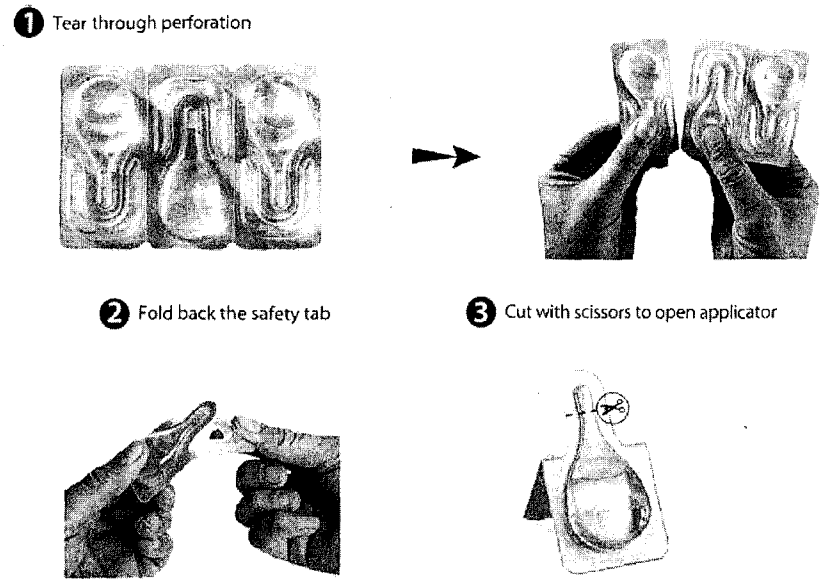
Side Effects: Monitor your dog after application. Side effects, although very rare, may include signs of skin irritation such as redness scratching, or other signs of discomfort. Gastrointestinal signs such as vomiting or diarrhea have also been reported. If these or other side effects (such as lethargy) occur, consult your veterinarian or call 1-800-999-0297. Have the product container or label with you when calling your veterinarian for advice.

DO NOT USE ON CATS. Keep cats away from treated dog for 24 hours. If applied to a cat or ingested by a cat, contact your veterinarian.

["Do Not Use on Cats" icon, 1.5cm x 1.5cm on final or as indicated]

Information in [ ] is optional

{For cartons containing [0.4mL (0.014 fl oz)] applicator tubes} Only For Dogs Weighing 3[-][to] 10 lbs. Do not apply to dogs weighing less than 3 lbs. [including small dogs and puppies, 7 weeks or older]
{For cartons containing 1.0 mL (0.034 fl oz)] applicator tubes} Only for Dogs Weighing 11 – 20 lbs (1.0 ml size)
{For cartons containing [2.5 mL (0.085 fl oz)] applicator tubes} Only for Dogs Weighing 21 – 55 lbs (2.5 ml size)
{For cartons containing [4.0 mL (0.135 fl oz)] applicator tubes} Only for Dogs Weighing > 55 lbs (4.0 ml size)



FREQUENCY OF APPLICATION

Treatment of [Brand Name] will kill fleas on dogs [and][puppies] within [twelve] [12] hours and[[re][infestation] within 2 hours]]. It is possible pre-existing pupae in the environment may continue to emerge for [[six] [6] weeks] [or longer] depending on climatic conditions. Use [brand name] [monthly] [every 30 days] [every 4 weeks] for the control and prevention of flea [[re]infestation]]. [[Studies have shown that] [brand name] kills fleas on dogs within 12 hours for up to [[4][four] weeks]] [1 month] [30 days]] and before fleas can start laying eggs. To prevent flea [re]infestation, apply monthly. [Brand Name] remains effective even after exposure to sunlight. [Brand name] is water resistant and still is effective, after bathing or water immersion. Allow treated area to dry thoroughly.

Information in [ ] is optional

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

PESTICIDE STORAGE: Store only in original container in a cool, dry area inaccessible to children and pets and away from heat and sunlight.

PESTICIDE DISPOSAL AND CONTAINER HANDLING: Nonrefillable container. Do not reuse or refill this container. **If empty:** Place in trash or offer for recycling, if available. **If partly filled:** Call your local solid waste agency for disposal instructions. Never place unused product down any indoor or outdoor drain.

LIMITED WARRANTY AND LIMITATION OF DAMAGES
Seller warrants that the material conforms to the chemical parameters of the US EPA registration and the label. To the extent consistent with applicable law, seller makes no warranty, express or implied, other than indicated on the label. Buyer and user assume all risk of use and handling of this material. To the extent consistent with applicable law, any damages arising from use of this product or a breach of this warranty shall be limited to direct damages and shall not include consequential or incidental damages such as loss of profit or values.

[Made in Germany]

[Distributed by:] [Manufactured by:]
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

EPA Reg. No. **83399**-NEW
EPA Est. No. **TBD**
[lot, date & label code] [UPC CODE]

[END - BACK / SIDE PANEL]

{Front Label}	{Back Label}
[Brand Name] **For Dogs** [3-10 (or) 11-20 (or) 21-55 (or) >55)] lbs and ≥7 wks Imidacloprid 9.10% Pyriproxyfen 0.46% 0.014 fl oz (or) 0.034 fl oz (or) 0.085 fl oz (or) 0.135 fl oz {label code}	KEEP OUT OF REACH OF CHILDREN WARNING: Read directions and precautions before using. Use scissors to open. EPA REG. No. 83399-NEW {label code}

{END TUBE / VIAL LABEL}

Information in [ ] is optional

Pages 138-146 Confidential Statement of Formula may be entitled to confidential treatment